APPENDIX A

UNITED STATES COURT OF APPEALS
DISTRICT OF COLUMBIA CIRCUIT

Nos. 00-5050 & 00-5396

ANDRX PHARMACEUTICALS, INC.,
Appellee,

v.

BIOVAIL CORPORATION INTERNATIONAL,
Appellant.

Argued February 12, 2001.
Decided July 31, 2001.

Appeals from the United States District Court for the District of Columbia (No. 98cv00099).

Before: HENDERSON, RANDOLPH and GARLAND, *Circuit Judges*.

KAREN LECRAFT HENDERSON, *Circuit Judge*:

Appellant Biovail Corporation (Biovail) appeals two district court decisions. One dismissed with prejudice its antitrust counterclaim against appellee Andrx Pharmaceuticals, Inc (Andrx). The second denied its motion for reconsideration of the court's dismissal. For the reasons that follow, we affirm the district court's dismissal of the counterclaim but reverse its decision to do so with prejudice.

I. Statutory Background

A company wishing to market a new drug must seek the approval of the United States Food & Drug Administration (FDA) by completing a "New Drug Application" (NDA). *See*

American Bioscience, Inc. v. Thompson, 243 F.3d 579, 580 (D.C.Cir.2001); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1063 (D.C.Cir.1998); *see also* 21 U.S.C. § 355(a) ("No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to (b) or (j) of this section is effective with respect to such drug."). An NDA is time-consuming and costly to prepare because it must include data from studies showing the drug's safety and effectiveness. *See Mova*, 140 F.3d at 1063. In 1984 the Congress enacted the Hatch-Waxman Amendments to the Food, Drug and Cosmetic Act (Amendments) to, *inter alia*, simplify the procedure for FDA approval. *See* Drug Price Competition and Patent Term Restoration Act of 1984, Pub.L. No. 98-417, 98 Stat. 1585 (1984) (codified in various sections of titles 21, 35 & 42 U.S.C.); *see generally* Allan M. Fox & Allan R. Bennett, *The Legislative History of the Drug and Patent Term Restoration Act of 1984*, at 259 (1987); James J. Wheaton, "Generic Competition and Pharmaceutical Innovation: the Drug Price Competition and Patent Term Restoration Act of 1984," 35 *Cath. Univ. L.Rev.* 433 (1986). Under the Amendments, the original applicant for FDA approval (the "pioneer" applicant) must still prepare an NDA. Subsequent applicants who wish to manufacture generic versions [1] of the pioneer drug, however, need only complete an Abbreviated New Drug Application (ANDA) that relies on the FDA's previous determination that the drug is safe and effective.[2] *See Mova*,

---

[1] A generic version of a pioneer drug (often described as a brandname drug) contains the same active ingredients, but not necessarily the same inactive ingredients, as the pioneer drug. A generic drug, as the name implies, is ordinarily sold without a brand name and at a lower price. *See United States v. Generix Drug Corp.*, 460 U.S. 453, 454-55, 103 S.Ct. 1298, 75 L.Ed.2d 198 (1983).

[2] Before the Amendments, an earlier version of the ANDA procedure was available to a generic drug manufacturer of a pioneer drug approved before 1962. A generic version of a pioneer drug approved after 1962,

140 F.3d at 1063. The generic drug share of the prescription drug market has grown from 19 per cent in 1983 to over 40 per cent in 1995. *See* Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry* ix (1998). In addition, almost all of the most popular pioneer drugs with expired patents now have generic versions available. *Id.* at xii.

Although the Congress was interested in increasing the availability of generic drugs, it also wanted to protect the patent rights of the pioneer applicants. *See* David A. Balto, *"Pharmaceutical Patent Settlements: The Antitrust Risks," 55 Food & Drug L.J. 321, 324 (2000).* The Amendments, therefore, require that an NDA contain a list of any patents "which claim[ ] the drug . . . or which claim[ ] a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1). The FDA maintains a record of such information in its publication entitled *Approved Drug Products with Therapeutic Equivalence*, commonly known as the Orange Book. *See* 21 U.S.C. § 355(j)(7)(A). For each patent applicable to the pioneer drug listed in the Orange Book, an ANDA applicant must certify whether the proposed generic drug would infringe that patent and, if not, why not. An ANDA applicant has four certification options. It may certify (1) that the required patent information has not been filed, (2) that the patent has expired, (3) that the patent has not expired but will expire on a particular date or (4) that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval. *See* 21 U.S.C. § 355(j)(2)(A)(vii). The last of these options, and the one relevant here, is the Paragraph IV certification.

---

however, could be approved only through a full NDA. *See* Fox & Bennett, *supra*, at 95.

After an applicant makes a Paragraph IV certification, the statute provides a 45-day window during which the patent holder may bring suit against the applicant. If the patent holder brings a timely suit, the statute bars the FDA from approving the applicant's ANDA, or any subsequent ANDA, for thirty months or until the successful resolution of the patent infringement suit, whichever is earlier, at which time the first ANDA applicant is eligible for FDA approval and upon such approval is awarded a 180-day exclusivity period in which to market its generic version. *See* 21 U.S.C. § 355(j)(5)(B)(iii). The statute permits the court to lengthen or shorten the 30-month waiting period if it determines that either party has failed to "reasonably cooperate in expediting the action." *Id.*[3]

---

[3] The full text of section 355(j)(5)(B)(iii) provides:

> If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—
>
> > (I) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,
> >
> > (II) if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of Title 35, or
> >
> > (III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from

II. Background

Hoechst Marion Roussel, Inc. (HMRI) is the manufacturer, marketer and patent holder of the brand name prescription drug Cardizem CD, which consists of a once-daily dosage of the chemical compound dilitiazem hydrochloride. Cardizem CD is widely prescribed for the treatment of chronic chest pains (angina) and hypertension and for the prevention of heart attacks and strokes. *See In re Cardizem CD Antitrust Litig.*, 105 F.Supp.2d 618, 622 (E.D.Mich.2000). On September 22, 1995 Andrx filed an ANDA with the FDA seeking approval to manufacture and sell a generic form of Cardizem CD. On December 31, 1995 it made the Paragraph IV certification with regard to all unexpired patents included in the Orange Book's Cardizem CD entry and certified that its generic form of Cardizem CD did not infringe the patents owned or controlled by HMRI or its affiliates. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV); 21 C.F.R. § 314.94(a)(12)(i)(A)(4). In early 1996 HMRI filed a timely suit against Andrx for patent infringement.[4] The filing of the suit triggered the statutory 30-month waiting period during which any

---

> engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of Title 28, for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

[4] Later in 1996 Faulding Inc. filed an ANDA with a Paragraph IV certification for its generic version of Cardizem CD. In January 1997 HMRI also filed suit against Faulding for patent infringement.

subsequent ANDA applicant, including Biovail, could not receive final approval of its generic version of Cardizem CD. *See* 21 U.S.C. § 355(j)(5)(B)(iii).

In June 1997 Biovail filed an ANDA with the Paragraph IV certification for its generic version of Cardizem CD but HMRI filed no patent infringement suit against it. On September 15, 1997 the FDA issued its tentative approval of Andrx's ANDA.[5] Nine days later, on September 24, 1997, HMRI and Andrx entered into an agreement (Agreement or HMRI-Andrx Agreement) purporting to maintain the status quo pending the outcome of HMRI's patent infringement suit against Andrx. Under the terms of the Agreement, Andrx agreed not to sell its generic version of Cardizem CD until a specific time agreed upon by the parties. It also agreed to diligently prosecute its ANDA and not to relinquish or otherwise compromise any right accruing thereunder. HMRI agreed to make interim payments to Andrx in the amount of $40 million per year, payable quarterly, beginning on the date Andrx's generic version of Cardizem CD received FDA approval and ending on the date Andrx either began to sell its generic version or was adjudged liable for patent infringement.

In early 1998 Andrx filed suit against the FDA and certain ANDA applicants (including Biovail) to clarify its right as the first to file an ANDA for Cardizem CD. The suit sought injunctive relief requiring the FDA to provide Andrx with "a period of 180 days of marketing exclusivity for its controlledrelease generic formulations of the drugs Dilacor XR and Cardizem CD." JA 13. It also requested injunctive relief prohibiting the FDA "from approving any ANDA submitted by defendant Biovail . . . for a generic version of Cardizem CD that contains a paragraph 4 certification until

---

[5] The FDA issued tentative, as opposed to final, approval due to the pending infringement suit and the resulting 30-month statutory waiting period.

180-days after Andrx begins marketing its generic formulation of Cardizem CD or a court enters a judgment in the patent litigation brought by HMRI in the Southern District of Florida, whichever is earlier." JA 22. Biovail counterclaimed, alleging that Andrx had violated sections 1 and 2 of the Sherman Act as well as New Jersey common law.[6]

On July 3, 1998 the FDA granted final approval to Andrx's ANDA for a generic version of Cardizem CD. JA 44. By then, the 30-month waiting period had expired and Andrx was no longer restricted under the statutory scheme from marketing and selling its generic drug. Andrx, however, did not do so and on July 9, 1998, pursuant to the Agreement, HMRI began making quarterly payments of $10 million to Andrx. By not marketing its generic version of Cardizem CD, Andrx did not trigger the 180-day market exclusivity period, which in turn prevented the FDA from giving final approval to any subsequently filed applications for competing generic versions of Cardizem CD.

Approximately one year later, HMRI and Andrx terminated their Agreement and entered into a stipulation settling the patent litigation. On June 23, 1999, Andrx then began to market its generic version and its 180-day exclusivity period

---

[6] On July 14, 1998 the FDA published a notice entitled "Guidance for Industry on 180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act; Availability," interpreting the Hatch-Waxman Amendments so as to give Andrx the relief it sought in its complaint. The Guidance explained that the FDA intended to delete the "successful defense" provisions from § 314.107(c)(1) and that the FDA would not enforce the "successful defense" provisions in the interim. *See* 63 Fed.Reg. 37,890 (July 14, 1998); *see also* JA 62 (Federal Defendant's Motion to Dismiss); JA 198 (Notice of Dismissal). Accordingly, the district court subsequently dismissed the complaint. *See* JA 199. Andrx had earlier moved to dismiss Biovail's counterclaim for failure to state a claim upon which relief may be granted because, *inter alia*, Biovail lacked standing to assert an antitrust violation.

began to run. In October 1999 the FDA gave tentative approval to Biovail's ANDA and final approval on December 23, 1999.[7] Neither Andrx nor Biovail, however, informed the district court of these developments. On January 6, 2000 the district court granted Andrx's Rule 12(b)(6) motion to dismiss Biovail's counterclaim, the federal antitrust counts with prejudice and the state law claims without prejudice. The court concluded that Biovail did not, and in fact could not, plead an antitrust injury causally linked to Andrx's alleged anticompetitive behavior. *Andrx Pharm., Inc. v. Friedman,* 83 F.Supp.2d 179, 185-87 (D.D.C.2000) ("Court cannot find that Biovail can establish that it has suffered 'antitrust injury.'"). On February 2, 2000 Biovail moved for reconsideration under FRCP 60(b) and on February 4, 2000 it filed a notice of appeal (No. 00-5050). The district court subsequently denied the motion for reconsideration and Biovail noticed its appeal of that decision (No. 00-5396) on November 3, 2000. This court granted Biovail's motion to consolidate the appeals.

III. Analysis

We give *de novo* review to a Rule 12(b)(6) dismissal. *See NRA v. Reno,* 216 F.3d 122, 126 (D.C.Cir.2000); *see also Amarel v. Connell,* 102 F.3d 1494, 1507 (9th Cir.1997) (holding that antitrust standing is question of law reviewed *de novo*). "The complaint should not be dismissed unless plaintiffs can prove no set of facts in support of their claim which would entitle them to relief." *Kowal v. MCI Communications Corp.*, 16 F.3d 1271, 1276 (D.C.Cir.1994). We liberally construe the complaint in the plaintiff's favor and grant the plaintiff the benefit of all inferences that can be

---

[7] In a letter dated October 22, 1999 the FDA explained to Biovail that it had "completed review" of its ANDA and found its generic "safe and effective." JA 322. It gave tentative, rather than final, approval because of "the exclusivity granted by the agency to Andrx." JA 323; *see also* JA 327.

derived from the facts alleged. "However, the court need not accept inferences drawn by plaintiffs if such inferences are unsupported by the facts set out in the complaint. Nor must the court accept legal conclusions cast in the form of factual allegations." *Id.* The court reviews the denial of the appellant's *Rule 60(b)* motion for abuse of discretion "unless the decision is 'rooted in an error of law.'" *United Mine Workers of Am.1974 Pension v. Pittston Co.*, 984 F.2d 469, 476 (D.C.Cir.1993) (citation omitted).

Section 4 of the Clayton Act provides that a private person "injured in his business or property by reason of anything forbidden in the antitrust laws . . . shall recover threefold the damages by him sustained, and the cost of suit, including a reasonable attorney's fee." 15 U.S.C. § 15(a). The Clayton Act includes the Sherman Act [8] as one of the "antitrust laws." See 15 U.S.C. § 12. A person "threatened [with] loss or damage by a violation of the antitrust laws" can seek injunctive relief under section 16 of the Clayton Act. 15 U.S.C. § 26. The availability of a private antitrust action, and its accompanying treble damages remedy, serves both to compensate private persons for their injuries and to punish wrongdoers. *See* 2 Phillip E. Areeda, Herbert Hovenkamp & Roger D. Blair, *Antitrust Law* § 330, at 273 (2d. ed.2000). Private enforcement of the nation's antitrust laws also increases the likelihood that violators will be discovered. *See Blue Shield of Va. v. McCready*, 457 U.S. 465, 473 n. 10, 102 S.Ct. 2540, 73 L.Ed.2d 149 (1982) ("Only by requiring

---

[8] Section 1 of the Sherman Act prohibits contracts, combinations or conspiracies "in restraint of trade or commerce among the several States, or with foreign nations." 15 U.S.C. § 1. Section 2 states that "[e]very person who shall monopolize, or attempt to monopolize, or combine or conspire with any other person or persons, to monopolize any part of the trade or commerce among the several States, or with foreign nations, shall be deemed guilty of a felony." 15 U.S.C. § 2. In its counterclaim, Biovail alleged that Andrx violated both sections 1 and 2 of the Sherman Act. JA 20-21.

violators to disgorge the 'fruits of their illegality' can the deterrent objectives of the antitrust laws be fully served.") (citation omitted). In fact, private enforcement actions account for the overwhelming majority of antitrust litigation in the United States. *See* William F. Dolan, *Developments in Private Antitrust Enforcement in 1999*, 1181 PLI/Corp 971, 975 (2000).

"On its face, § 4 contains little in the way of restrictive language." *Reiter v. Sonotone Corp.*, 442 U.S. 330, 337, 99 S.Ct. 2326, 60 L.Ed.2d 931 (1979). "The statute does not confine its protection to consumers, or to purchasers, or to competitors, or to sellers. . . . The Act is comprehensive in its terms and coverage, protecting all who are made victims of the forbidden practices by whomever they may be perpetrated." *Mandeville Island Farms, Inc. v. American Crystal Sugar Co.*, 334 U.S. 219, 236, 68 S.Ct. 996, 92 L.Ed. 1328 (1948). The Supreme Court, however, has recognized that "the potency of the remedy implies the need for some care in its application" and does not construe the section 4 language to allow suit by *every* party affected by an antitrust violator's "ripples of harm." *McCready*, 457 U.S. at 476-77. An antitrust plaintiff must establish an injury-in-fact or a threatened injury-in-fact caused by the defendant's alleged wrongdoing. *See Associated Gen. Contractors of Cal., Inc. v. California State Council of Carpenters*, 459 U.S. 519, 535, 103 S.Ct. 897, 74 L.Ed.2d 723 (1983). Moreover, the injury must affect the plaintiff's business or property and must be the kind of injury the antitrust laws were intended to prevent; it must "flow[ ] from that which makes defendants' acts unlawful." *Brunswick Corp. v. Pueblo Bowl-O-Mat, Inc.*, 429 U.S. 477, 489, 97 S.Ct. 690, 50 L.Ed.2d 701 (1977). Additional factors to be considered in determining whether the plaintiff has "antitrust standing" include: the directness of the injury, whether the claim for damages is "speculative," the existence of more direct victims, the potential for duplicative recovery and the complexity of apportioning damages. *See*

Associated Gen. Contractors, 459 U.S. at 542-45; *see also Adams v. Pan Am. World Airways, Inc.*, 828 F.2d 24, 26 (D.C.Cir.1987). We review the district court's decision dismissing Biovail's antitrust counterclaim *with prejudice* in light of these standing requirements.

A. Injury-in-Fact and Causation

As in any civil action for damages, the plaintiff in a private antitrust lawsuit must show that the defendant's illegal conduct caused its injury. *See* 2 Areeda et al., *supra*, § 338, at 316; *see also Restatement (Second) of Torts* §§ 431, 433 (1965). The plaintiff's first step is to plead an injury- in-fact or, in a suit for equitable relief, a threatened injury-in-fact to business or property.[9] *See Hecht v. Pro-Football, Inc.*, 570 F.2d 982, 993 (D.C.Cir.1977). The "burden of proving the fact of damage under § 4 of the Clayton Act is satisfied by [ ] proof of *some* damage flowing from the unlawful conspiracy; inquiry beyond this minimum point goes only to the amount and not the fact of damage." *Zenith Radio Corp. v. Hazeltine Research, Inc.*, 395 U.S. 100, 114 n. 9, 89 S.Ct. 1562, 23 L.Ed.2d 129 (1969) (emphasis original). The district court held that Biovail not only failed to plead an injury or a threatened injury but also was unable to do so because Biovail had yet to receive FDA approval for its generic version of Cardizem CD and gave no assurance that it would have entered the market had it gained approval. *Cf. Indium*

---

[9] Section 4 of the Clayton Act authorizes a private suit only for injury to "business or property." 15 U.S.C. § 15; *see* 2 Areeda *et al.*, *supra*, § 336, at 303. At the very least, "business or property" includes "commercial interests or enterprises." *Hawaii v. Standard Oil Co.*, 405 U.S. 251, 264, 92 S.Ct. 885, 31 L.Ed.2d 184 (1972). In *Reiter v. Sonotone Corp.*, the Supreme Court noted that "the word 'property' has a naturally broad and inclusive meaning." *Id.* at 338. On appeal, the parties do not raise the issue of whether Biovail sufficiently alleged an injury to "business or property."

Corp. of Am. v. Semi-Alloys, Inc., 781 F.2d 879, 882 (Fed.Cir.1985) (because plaintiff was not prepared to enter market, defendant's conduct caused no injury).

When competitors violate the antitrust laws and another competitor is forced from a market, the latter suffers an injury-in-fact. A competitor that has not yet entered the market may also suffer injury but courts require a "potential" competitor to demonstrate both its intention to enter the market and its preparedness to do so. *See Hecht*, 570 F.2d at 987, 994 ("[A] potential competitor cannot achieve standing merely by demonstrating his intention to enter a field; he must also demonstrate his preparedness to do so." (emphasis original)); *see Indium Corp.*, 781 F.2d at 882 (no injury if plaintiff not prepared to enter market). "Indicia of preparedness include adequate background and experience in the new field, sufficient financial capability to enter it, and the taking of actual and substantial affirmative steps toward entry, 'such as the consummation of relevant contracts and procurement of necessary facilities and equipment.'" *Hecht*, 570 F.2d at 994 (footnote and citation omitted). Thus, in evaluating whether Biovail sufficiently pleaded or *can* sufficiently plead an injury or threatened injury, we must examine its intent and preparedness to enter the market from which it alleges it was excluded, that is, the Cardizem CD, or controlled-release dilitiazem-based drug, market.

In the pharmaceutical industry, FDA approval is a prerequisite to enter any drug market. *See* 21 U.S.C. § 355(a) ("No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug."). The district court concluded that Biovail suffered no injury as a result of the HMRI-Andrx Agreement "because *even today*, Biovail *could not go to market with a generic version of Cardizem*,

because it had not received FDA approval." [10] *Andrx Pharm.*, 83 F.Supp.2d at 186 (emphasis original). The only facts Biovail alleged to support its claim of injury were that the Agreement "prevent[ed] generic Cardizem CD products by Biovail and others from reaching the market as soon as they would otherwise be allowed," JA 44 (§ 19), and that Biovail had filed an ANDA for a generic version of Cardizem CD, JA 50 (§ 41). Biovail did not explicitly allege that it was prepared to bring a generic version of Cardizem CD to market or that it anticipated FDA approval. In addition, when the FDA eventually approved its ANDA, Biovail inexplicably failed to inform the district court. Based on Biovail's failure to plead sufficient intent and preparedness to enter the market, the district court dismissed Biovail's antitrust counterclaim.[11] *See Andrx Pharm.*, 83 F.Supp.2d at 187.

The district court, however, went beyond dismissing the counterclaim based on the pleading's insufficiency. It dismissed Biovail's antitrust counterclaim *with prejudice*. n so doing it decided, as a matter of law, that Biovail was unable to set forth any set of facts that would entitle it to the relief it sought. "[D]ismissal with prejudice should be granted only when a trial court determines that 'the allegation of other facts consistent with the challenged pleading could not possibly cure the deficiency.'" *Jarrell v. United States Post. Serv.*, 753 F.2d 1088, 1091 (D.C.Cir.1985) (quoting *Bonnano v. Thomas*, 309 F.2d 320, 322 (9th Cir.1962)). The district court did not conclude that Biovail did not intend to

---

[10] By the time of the district court's decision, however, the FDA had approved Biovail's ANDA for its generic version of Cardizem CD although the court was not apprised of that development.

[11] The issues of injury-in-fact and causation are closely linked on this point. By not alleging facts indicating its intent and preparedness to enter the Cardizem CD market, Biovail failed to allege both an injury (no loss of profits because not prepared to enter market) and causation (any damages not related to HMRI-Andrx Agreement because Agreement did not cause loss of profits).

enter the market or that it was not sufficiently prepared to do so but instead that it had not sufficiently alleged its intent and capacity to enter the market. *See Andrx Pharm., Inc.*, 83F.Supp.2d at 184-85. Its statement that the FDA had not yet approved Biovail's ANDA as of the date of its ruling was understandable in light of the parties' failure to inform the court to the contrary but the statement was nonetheless erroneous and not a ground to dismiss with prejudice.

As its motion for reconsideration manifests, Biovail *can* allege facts sufficient to indicate its intent and preparedness. *See* JA 297, 300-02. And even before the FDA approved Biovail's ANDA, Biovail could have alleged its intent and preparedness to enter the market by claiming that FDA approval was probable. Andrx's original suit, which sought to enjoin the FDA from approving Biovail's ANDA, suggests that Biovail (or so Andrx believed) may have intended and been sufficiently prepared to enter the market. *See Zenith Radio*, 395 U.S. at 130 ("[Section 16] authorizes injunctive relief upon the demonstration of 'threatened' injury. That remedy is characteristically available even though the plaintiff has not yet suffered actual injury; he need only demonstrate a significant threat of injury from an impending violation of the antitrust laws or from a contemporary violation likely to continue or recur.") (citation and footnote omitted); *L.A. Mem'l Coliseum Comm'n v. National Football League*, 468F.Supp. 154, 159 (C.D. Cal.1979). And unlike the plaintiffs in *Confederate Memorial Association, Inc. v. Hines*, 995 F.2d 295 (D.C.Cir.1993), where this court upheld the trial court's dismissal with prejudice of the plaintiffs' RICO claims because the plaintiffs failed to allude to facts "entitling them to recover," Biovail has (in its motion for reconsideration) alluded to facts—FDA approval and intent to enter market—that may entitle it to relief. *Id.* at 299; *cf. Askins v. District of Columbia*, 877 F.2d 94, 99 (D.C.Cir.1989) (dismissal with prejudice of unripe legal

claim is legal error). Because Biovail may be able to cure its pleading deficiency, we conclude that dismissal with prejudice was erroneously granted.

Andrx responds, however, that an independent legal ground supports dismissal with prejudice. It argues Biovail is unable to allege causation. To sufficiently plead causation, a plaintiff must allege that the defendant violated the antitrust laws, that the defendant's alleged violation "had a tendency to injure" the plaintiff's business or property, *Amerinet, Inc. v. Xerox Corp.*, 972 F.2d 1483, 1495 (8th Cir.1992), and that the plaintiff suffered a decline in its business or property "not shown to be attributable to other causes." *Bigelow v. RKO Radio Pictures, Inc.*, 327 U.S. 251, 264, 66 S.Ct. 574, 90 L.Ed. 652 (1945). The Supreme Court has explained "[i]t is enough that the illegality is shown to be a material cause of the injury; a plaintiff need not exhaust all possible alternative sources of injury in fulfilling his burden of proving compensable injury under [section 4 of the Clayton Act]." *Zenith Radio*, 395 U.S. at 114 n. 9.

The district court found that Biovail failed to establish the requisite causal connection between its injury and the alleged anticompetitive conduct. It concluded that any injury Biovail may have suffered was caused not by the HMRI-Andrx Agreement but instead by the lack of FDA approval of its generic version of Cardizem CD and by the delay period prescribed by the Hatch-Waxman Amendments. We disagree. Although we affirm the district court's dismissal to the extent Biovail failed to allege an injury-in-fact, we disagree with its conclusion that any injury Biovail might plead would be caused by "the existence of a troublesome statutory scheme that prohibits it from marketing a drug until the first ANDA recipient goes to market, and which places no restrictions on when, or even whether, that applicant must to *[sic]* go to market." *Andrx Pharms.*, 83 F.Supp.2d at 185. We also reject Andrx's argument that any rational actor like

itself would not market its generic drug until the patent infringement suit against it was resolved, making any loss of profits caused by Biovail's exclusion from the market a result of the statutory scheme, not Andrx's conduct. A reasonable juror could conclude that Andrx's argument contradicts the very premise of the HMRI-Andrx Agreement. Under the Agreement, HMRI paid Andrx 10 million dollars per quarter effectively not to enter the market. One can fairly infer from these facts, which were alleged in the counterclaim, that but for the Agreement, Andrx would have entered the market. As one commentator has noted, "[a] payment flowing from the innovator to the challenging generic firm may suggest strongly the anticompetitive intent of the parties in entering the agreement and the rent-preserving effect of that agreement." Balto, *supra*, at 335.

Andrx, however, argues that it "did nothing other than to act in accordance with rights granted to it under the Hatch-Waxman [Amendments]. The exercise of these statutory rights, exclusionary though they may be, cannot support a claim under the antitrust laws." Appellee Br. 31. Andrx may be correct that "[a] plaintiff cannot be injured in fact by private conduct excluding him from the market when a statute prevents him from entering that market in any event." *City of Pittsburgh v. West Penn Power Co.*, 147 F.3d 256, 268 (3d Cir.1998) (quoting Philip E. Areeda & Herbert Hovenkamp, *Antitrust Law*, § 363(b) at 222 (1995)). Although the Hatch-Waxman Amendments provide a 180-day period of market exclusivity to the first applicant to file an ANDA for a generic version of a pioneer drug, *see* 21 U.S.C. § 355(j)(5)(B)(iv),[12] through the Amendments, "Congress

---

[12] Section 355(j)(5)(B)(iv) provides:

> If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing

sought to get generic drugs into the hands of patients at reasonable prices—fast." *In re Barr Lab., Inc.*, 930 F.2d 72, 76 (D.C.Cir.1991). We disagree with Andrx that "its conduct was not only permitted under but clearly contemplated by the Hatch-Waxman" Amendments. Appellee Br. 32. Although it is true that the first to file an ANDA is permitted to delay marketing as long as it likes, the statutory scheme does not envision the first applicant's agreeing with the patent holder of the pioneer drug to delay the start of the 180-day exclusivity period. *See Mova Pharm.*, 140 F.3d at 1072 (acknowledging and describing as anomaly fact situation here presented).[13]

By accepting payments from HMRI, Andrx received the benefit of the 180-day exclusivity period without starting the clock. By agreeing with HMRI to share HMRI's profits from

---

such a certification, the application shall be made effective not earlier than one hundred and eighty days after—

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.

[13] The court stated in a footnote:

An *amicus* brief filed by Biovail Corporation International dramatically illustrates an analogous risk, not necessarily involving collusion. Biovail was the second applicant to file a paragraph IV ANDA for a generic version of a heart medication. Biovail was not sued by the pioneer drug company. The first applicant and the pioneer drug company are now in litigation, and, Biovail claims, the pioneer is paying the first applicant some $10 million per quarter in exchange for the first applicant's agreement not to sell its product after the 30-month waiting period expires. Under these circumstances, neither party would seem to have maximum incentive to bring the litigation to a close.

Id. at 1072 n. 14.

the sale of Cardizem CD, it was able to exclude other competitors from entering the market. Andrx's commitment not to trigger the running of the 180-day exclusivity period could have caused Biovail's injury (assuming FDA approval was probable and it was sufficiently prepared to enter the market) by denying it the ability to proceed to market with its own generic version. Although the 180-day provision of the Hatch-Waxman Amendments legally barred it from selling its product, Andrx's manipulation of the exclusivity period trigger date extended the legal bar.

Andrx maintains that the Agreement was not a restraint cognizable under the antitrust laws because, under the FDA regulations in effect at the time, it could not have caused the delay of FDA approval of Biovail's ANDA. In September 1997 (when the Agreement was signed) Andrx contends that the FDA regulations provided that the first ANDA applicant to file a Paragraph IV certification would not be granted a 180-day exclusivity period unless it had "successfully defended" any patent infringement action brought by the patent holder "before a subsequent applicant's ANDA was ready to be approved." Appellee Br. 37-38 (citing 21 C.F.R. § 314.107(c)(i) (1997)). We rejected the FDA's "successful defense" regulation in *Mova Pharm.*, 140 F.3d at 1076. Andrx argues that before the court invalidated the regulation, it could have done nothing to prolong its exclusivity period by delaying FDA approval of Biovail's ANDA because it was entitled to the exclusionary period only if it successfully defended the patent litigation before the FDA approved a subsequent applicant's ANDA. Had the FDA approved Biovail's ANDA, Andrx asserts, the Agreement would not have prevented Biovail from entering the market under the old regulation.

We reject this argument. On January 23, 1997 the district court in *Mova* issued a preliminary injunction against the FDA, holding that its "successful defense" regulation was inconsistent with the plain language of the statute and

therefore unenforceable. *See Mova Pharm. Corp. v. Shalala*, 955 F.Supp. 128, 131-32 (D.D.C.1997). HMRI and Andrx did not enter into their agreement until September 1997, almost nine months after the court's ruling. On April 14, 1998 this court affirmed the district court. *Mova*, 140 F.3d at 1076. The Agreement did not go into effect until three months later, in July 1998. The timing of the Agreement and of the demise of the successful defense requirement defeats Andrx's argument on this point.

Andrx nevertheless relies on the holding in *Polk Bros., Inc. v. Forest City Enters., Inc.*, 776 F.2d 185 (7th Cir.1985). In *Polk Bros.*, two companies, one that sold appliances and home furnishings and the other that sold building materials, lumber, tools and related products, reached an agreement to build on a large parcel of land one building, partitioned on the interior, to house both stores. *Id.* at 187. The arrangement was attractive to both firms due to the complementary nature of their products. They feared, however, that one day competition might replace cooperation so they negotiated a covenant restricting the products each could sell. *Id.* Years later one of the firms wanted to sell certain products in violation of the covenant and challenged the covenant on antitrust grounds when the other firm sought to enforce it. *Id.* at 187-88. Although the case arose under Illinois antitrust law, state law used federal antitrust law as a guide. *Id.* at 188. The Seventh Circuit upheld the validity of the covenant on the ground that, although "naked" restraints on trade are unlawful *per se*, ancillary restraints that facilitate productive activity are not. The court provided the following example:

> If A hires B as a salesman and passes customer lists to B, then B's reciprocal covenant not to compete with A is "ancillary." At the time A and B strike their bargain, the enterprise (viewed as a whole) expands output and competition by putting B to work. The covenant not to compete means that A may trust B with broader

> responsibilities, the better to compete against third parties. Covenants of this type are evaluated under the Rule of Reason as ancillary restraints, and unless they bring a large market share under a single firm's control they are lawful. *See United States v. Addyston Pipe & Steel Co.*, 85 F. 271, 280-83 (6th Cir.1898) (Taft, J.), *aff'd*, 172 U.S. 211 (1899).

Id. at 189. Thus even were we to adopt Andrx's characterization of the Agreement as "designed to preserve the *status quo* by duplicating relief that the court could have ordered had HMR[I] proceeded with" its motion for a preliminary injunction in the patent infringement litigation, the Agreement's allegedly anticompetitive provisions, including Andrx's pledge to continue to pursue its ANDA so as to forestall other applicants from receiving final FDA approval, were not necessarily ancillary restraints but rather could reasonably be viewed as an attempt to allocate market share and preserve monopolistic conditions.

Finally, Andrx contends that there were reasonable alternatives available to Biovail that could have avoided the exclusionary effect of the Agreement by triggering the 180-day period. Andrx relies on *CBS Broad. Sys., Inc. v. ASCAP*, 620 F.2d 930, 935 (2d Cir.1980), which held that "a practice that is not a *per se* violation . . . does not restrain trade when the complaining consumer elects to use it in preference to realistically available marketing alternatives." There the court found that to avoid injury, the consumer plaintiff had only to do nothing "more extraordinary than offer to buy from competing sellers." *Id.* at 936. Andrx argues that Biovail had two alternatives in lieu of waiting for Andrx to market its generic version of Cardizem CD. First, Biovail could have triggered the start of the 180-day exclusivity period itself under the "court decision" prong of the Hatch-Waxman Amendments, 21 U.S.C. § 355(j)(5)(B)(iv)(II), by seeking a declaratory judgment of non-infringement or invalidity of

HMRI's patent. The successful resolution (or dismissal) of the declaratory judgment action would have started the 180-day exclusivity period. *See Teva Pharm. USA, Inc. v. FDA*, 182 F.3d 1003, 1007-08 (D.C.Cir.1999). Alternatively, Biovail could have petitioned the FDA to nullify Andrx's 180-day exclusivity period. FDA regulations provide that "if FDA concludes that the applicant submitting the first application is not actively pursuing approval of its abbreviated application, FDA will make the approval of subsequent abbreviated applications immediately effective if they are otherwise eligible for an immediately effective approval." 21 C.F.R. § 314.107(c)(3).

The *CBS* holding is easily distinguishable; the language on which Andrx relies appears in the context of determining whether an agreement determined not to be *per se* unlawful nonetheless restrains trade on the facts. There the agreement benefitted the consumer by bundling various music copyright licenses, relieving the consumer of having to negotiate licenses with every individual artist. Andrx has cited no consumer benefit here. Biovail could have sought a decaratory judgment; however, as evidenced by the HMRI-Andrx patent infringement litigation, the time involved to obtain such a judgment made this option less than "fully available." *CBS*, 620 F.2d at 935. Likewise, as long as Andrx was pursuing FDA approval, Biovail could not use 21 C.F.R. § 314.107(c)(3) to revoke the 180-day exclusivity period. Indeed, according to the HMRI-Andrx Agreement, Andrx was to continue to pursue approval, which prevented the FDA from denying it the 180-day exclusivity period. Accordingly, we conclude the district court erred in dismissing *with prejudice* Biovail's counterclaim for failure to plead injury caused by Andrx's alleged unlawful restraint of trade. *See supra* note 8.

B. Antitrust Injury

"A private antitrust plaintiff does not acquire standing merely by showing that it was injured in a proximate and reasonably measurable way by conduct of the defendant violating the antitrust laws (injury-in-fact). Nor is it enough that the injury be causally connected to the acts that violate the antitrust laws (causation)." 2 Areeda *et al.*, *supra*, § 337a, at 305. In *Brunswick*, the Supreme Court explained that "[p]laintiffs must [also] prove *antitrust* injury, which is to say injury of the type the antitrust laws were intended to prevent and that flows from that which makes defendants' acts unlawful." 429 U.S. at 489 (emphasis original). "The injury should reflect the anticompetitive effect either of the violation or of anticompetitive acts made possible by the violation. It should, in short, be 'the type of loss that the claimed violations . . . would be likely to cause.'" *Id.* (quoting *Zenith Radio*, 395 U.S. at 125).[14] The Supreme Court has declared that the antitrust laws "were enacted for 'the protection of *competition* not *competitors*.'" *Id.* at 488 (quoting *Brown Shoe Co. v. United States*, 370 U.S. 294, 320, 82 S.Ct. 1502, 8 L.Ed.2d 510 (1962)) (emphasis original). Thus a competitor may not claim an injury resulting from competition even when such competition was actually caused by conduct that violates the antitrust laws. *See* 2 Areeda *et al.*, *supra*, § 337, at 306; *see also Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 596 n. 20, 106 S.Ct. 1348, 89 L.Ed.2d 538 (1986) (competitors suffer no harm from conspiracy to raise prices); *J. Truett Payne Co. v. Chrysler*

---

[14] In a suit for equitable relief under section 16 of the Clayton Act, the plaintiff must also establish an antitrust injury, although the injury need only be threatened. *See Zenith Radio*, 395 U.S. 130 (section 16 "invokes traditional principles of equity and authorizes injunctive relief upon the demonstration of 'threatened' injury"); *see also Cargill, Inc. v. Monfort of Colo., Inc.*, 479 U.S. 104, 122, 107 S.Ct. 484, 93 L.Ed.2d 427 (1986).

Motors Corp., 451 U.S. 557, 568, 101 S.Ct. 1923, 68 L.Ed.2d 442 (1981) (violation of antitrust laws not enough to confer standing).

In asserting that Biovail cannot assert an antitrust injury, Andrx compares it to the *Brunswick* plaintiffs. In *Brunswick*, the plaintiffs, three bowling alleys, complained that the defendant's acquisition of several financially troubled bowling centers violated section 7 of the Clayton Act. In seeking damages, the plaintiffs "attempted to show that had [the defendant] allowed the defaulting centers to close, [the plaintiffs'] profits would have increased." *Brunswick*, 429 U.S. at 481. The Supreme Court held that even though the plaintiffs' injury—loss of profits—was caused by the defendant's potentially unlawful acquisitions, the plaintiffs suffered no antitrust injury because the increased competition resulting from the defendant's purchase and operation of competing bowling alleys was not an injury antitrust laws were designed to prevent. *Id.* at 488. The Court explained that the plaintiffs' injury resulted from competitive, not anticompetitive, conduct. Further, because the plaintiffs would have suffered the same injury had their rivals been lawfully acquired by someone else, their injury did not occur "'by reason of anything forbidden in the antitrust laws': while [plaintiffs'] loss occurred 'by reason of' the unlawful acquisitions, it did not occur 'by reason of' that which made the acquisitions unlawful." *Id.* Unlike the *Brunswick* plaintiffs' injury, Biovail's alleged injury is the type the antitrust laws were designed to prevent. If Biovail's allegations are correct, the Andrx-HMRI Agreement neither enhanced competition nor benefitted consumers; if anything, it accomplished just the opposite by preserving HMRI's monopoly. Moreover, Biovail alleged that its exclusion from the market occurred not only by reason of the unlawful Agreement but also by reason of that which made the Agreement unlawful, that is, an illegal restraint of trade. *See Brunswick*, 429 U.S. at 488.

Andrx next argues that it could have lawfully excluded Biovail from the Cardizem CD market by deciding, on its own, to delay marketing of its generic version of Cardizem CD and therefore Biovail's alleged injury does not constitute an antitrust injury. It contends that because its underlying conduct was legal, the fact that it combined to act that way cannot give rise to an antitrust violation. *See ES Dev., Inc. v. RWM Enters., Inc.*, 939 F.2d 547, 553 (8th Cir.1991) (explaining that "[t]he evidence must also establish that the alleged participants combined or conspired to 'achieve an unlawful objective'"). Under the Hatch-Waxman Amendments, Andrx was lawfully entitled to unilaterally delay marketing its product until the patent infringement claims against it were resolved. Although its *unilateral* decision not to market its generic version of Cardizem CD would have prevented others, including Biovail, from entering the market, the counterclaim alleges that Andrx entered into an anticompetitive *agreement* with HMRI in order to exclude others; HMRI's ten million dollar quarterly payments were presumably in return for something that Andrx would not otherwise do, that is, delay marketing of its generic. Andrx's argument that any rational actor would wait for resolution of the patent infringement suit is belied by the *quid* of HMRI's *quo*. *See* 54 Fed.Reg. 42,873, 42,882-83 ("[I]t can be mutually beneficial for the innovator and the generic company that is awarded 180 days of generic exclusivity to enter into agreements that block generic competition for extended periods. This delayed competition harms consumers by slowing the introduction of lower priced products into the market and thwarts the intent of the Hatch-Waxman Amendments.").[15]

---

[15] The statutorily granted monopoly of patent rights is similar. Like a drug's 180-day exclusive market period, a patent grant in and of itself is "an exception to the general rule against monopolies and to the right to a free and open market." *Walker Process Equip., Inc. v. Food Mach. &*

Antitrust law looks at entry into the market as one mechanism to limit and deter exploitation of market power by those who may temporarily possess it. "Existing firms know that if they collude or exercise market power to charge supracompetitive prices, entry by firms currently not competing in the market becomes likely, thereby increasing the pressure on them to act competitively." *FTC v. H.J. Heinz Co.*, 246 F.3d 708, 717 n. 13 (D.C.Cir.2001). The FDA acknowledges that "[u]nder current regulatory provisions, the first generic applicant to file a substantially complete ANDA with a paragraph IV certification can delay generic competition by entering into certain commercial arrangements with an innovator company." 64 Fed.Reg. 42,882.[16] Such an arrangement can manipulate the statutory

---

Chem. Corp., 382 U.S. 172, 177, 86 S.Ct. 347, 15 L.Ed.2d 247 (1965) (quoting *Precision Instrument Mfg. Co. v. Automotive Maintenance Mach. Co.*, 324 U.S. 806, 816, 65 S.Ct. 993, 89 L.Ed. 1381 (1945)). But even a patent-right holder is not immune from antitrust liability. In *United States v. Singer Mfg. Co.*, 374 U.S. 174, 83 S.Ct. 1773, 10 L.Ed.2d 823 (1963), two competitors, Singer and Gegauf, entered into a cross-licensing agreement to settle a Patent Office interference proceeding involving their conflicting patent claims. Although Singer (like Andrx) had no obligation to pursue a patent grant and could have, on its own, withdrawn from the interference proceeding, it nevertheless acted unlawfully when it agreed with a competitor to settle the dispute, suppress information and exclude others from the market. *See id.* at 196; *see also American Cyanimid Co.*, 72 F.T.C. 623 (1967), *aff'd sub nom. Charles Pfizer & Co. v. FTC*, 401 F.2d 574 (6th Cir.1968) (Tetracycline case).

[16] The FDA has proposed a "triggering period" during which there must exist either a favorable court decision regarding the alleged infringed patent or the first applicant must begin commercial marketing. If the first applicant does neither, it forfeits its 180-day exclusivity period. *See* 64 Fed.Reg. 42,877. "In most cases, the triggering period would begin to run on the day a subsequent ANDA applicant with a paragraph IV certification receives a tentative approval stating that but for the first applicant's exclusivity, the subsequent ANDA would receive final approval." *Id.* The triggering period would also begin to run upon expiration of any 30-month stay in place.

grant of a monopoly to bar competitive entries. *See* Balto, *supra*, at 331 ("The competitive concern is that the 180-day exclusivity provision can be used strategically by a patent holder to prolong its market power in ways that go beyond the intent of the patent laws and the Hatch-Waxman Act by delaying generic entry for a substantial period."). Andrx argues that the Agreement merely preserved the status quo—in effect a stipulated preliminary injunction—until the conclusion of the patent infringement suit. When the court grants preliminary injunctive relief, however, it does so only after considering the public interest and the likelihood of success on the merits. *See Washington Metro. Area Transit Comm'n v. Holiday Tours, Inc.*, 559 F.2d 841, 842-43 (D.C.Cir.1977); *accord Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1317-18 (D.C.Cir.1998); *CityFed Fin. Corp. v. Office of Thrift Supervision*, 58 F.3d 738, 746-47 (D.C.Cir.1995).[17] Moreover, even if Andrx's agreement to maintain the status quo was lawful, its commitment to continue to prosecute its ANDA and do nothing to jeopardize its 180-day exclusivity period went beyond preserving the status quo. "To be ancillary, and hence exempt from the per se rule, an agreement eliminating competition must be subordinate and collateral to a separate, legitimate transaction. . . . If [the restraint] is so broad that part of the restraint suppresses competition without creating efficiency, the restraint is, to that extent, not ancillary." *Rothery Storage & Van Co. v. Atlas Van Lines, Inc.*, 792 F.2d 210, 224 (D.C.Cir.1986). As Biovail has pleaded the facts, HMRI and

---

[17] By contrast, a private agreement purporting to maintain the status quo may not be in the public interest or may have little likelihood of success on review. *See generally* Sheila F. Anthony, *Prepared Remarks before the ABA "Antitrust and Intellectual Property: The Crossroads" Program, Riddles and Lessons from the Prescription Drug Wars: Antitrust Implications of Certain Types of Agreements Involving Intellectual Property* (June 1, 2000), available at www.ftc.gov/speeches/anthony/sfip000601.htm.

Andrx combined to achieve an unlawful objective, namely, the extension of the exclusivity period granted under the Hatch-Waxman Amendments. Accordingly, we conclude that Biovail can allege an antitrust injury, that is, one the antitrust laws were designed to prevent and that flows from that which makes the defendant's conduct unlawful.

C. Speculative Nature of Harm

Standing may yet be denied if damages "rest[ ] at bottom on some abstract conception or speculative measure of harm." *McCready*, 457 U.S. at 475 n. 11. In *Associated General Contractors*, the Court denied standing because the plaintiff's damages claim was "highly speculative." 459 U.S. at 542; *accord Adams*, 828 F.2d at 30. It noted that the plaintiff union did not allege (1) that any of its collective bargaining agreements were terminated as a result of the defendant's alleged anticompetitive acts, (2) that union firms' aggregate share of the contracting market had been diminished and (3) that its revenue from dues and initiation fees had decreased. On the other hand, in *Bigelow*, the Court held that the plaintiff's damages were not too speculative to support the jury's verdict of damages. 327 U.S. at 265. There, the movie theater owner plaintiffs claimed that defendant distributors and affiliated movie theaters conspired to prevent the plaintiffs from obtaining movies for their theaters until after the defendant theaters had shown them. *Id.* at 254. The Court permitted the jury to consider evidence of decline in prices, profits and values not shown to be attributable to other causes to calculate the quantum of damage caused by the defendants' unlawful acts. *Id.* at 264.

We find Biovail's damages claim, assuming it can plead its intent and preparedness to enter the market, more like that in *Bigelow* than in *Associated General Contractors*. According to its counterclaim, Biovail was not an inexperienced newcomer; it already manufactured generic pharmaceuticals. It had already developed its product and, once FDA gave

tentative approval to its ANDA, was simply waiting out Andrx's 180-day exclusivity period.[18] Although damages may be difficult to quantify, "[t]he most elementary conceptions of justice and public policy require that the wrongdoer shall bear the risk of the uncertainty which his own wrong has created." *Bigelow*, 327 U.S. at 265; *see Story Parchment Co. v. Paterson Parchment Paper Co.*, 282 U.S. 555, 562, 51 S.Ct. 248, 75 L.Ed. 544 (1931). Biovail may ultimately fail to establish the amount of damages beyond a nominal amount, *see Associated Gen. Contractors*, 459 U.S. at 544-45, but Biovail could continue to seek (if not moot) injunctive relief. *See Blue Cross & Blue Shield of Wis. v. Marshfield Clinic*, 152 F.3d 588, 595 (7th Cir.1998).[19]

---

[18] Biovail received tentative approval in October 1999. On November 5, 1999 Andrx petitioned for reconsideration and for a stay of the FDA's tentative approval. The parties dispute the effect of the petition on the timing of Biovail's final approval on December 23, 1999. Even if Biovail's damages period were relatively short, Biovail would nevertheless be able to seek recovery. Moreover, "[d]ifficulty of ascertainment [should not be] confused with right of recovery." *McCready*, 457 U.S. at 475 n. 11 (quoting *Bigelow*, 327 U.S. at 265).

[19] Antitrust standing also requires proximity between the alleged cause and the alleged injury. *See Associated Gen.Contractors*, 459 U.S. at 540; *McCready*, 457 U.S. at 476-77 ("'[D]espite the broad wording of § 4 there is a point beyond which the wrongdoer should not be held liable.'" (citation omitted)); 2 Areeda *et al.*, *supra*, § 339, at 325-26. In evaluating whether an injury is too remote, "we look (1) to the physical and economic nexus between the alleged violation and the harm to the plaintiff, and (2), more particularly, to the relationship of the injury alleged with those forms of injury about which Congress was likely to have been concerned in making defendant's conduct unlawful and in providing a private remedy under § 4." *McCready*, 457 U.S. at 478; *see In re Multidistrict Vehicle Air Pollution M.D.L.*, 481 F.2d 122, 129 (9th Cir.1973). In *McCready*, the Supreme Court held that health insurance subscribers had standing to sue their insurance company for colluding with physicians and psychiatrists to deny them reimbursement for payments made to psychologists. The Court acknowledged that while the psychologists (not the patients) were the targets of the conspiracy,

D. Existence of More Appropriate Plaintiff

In evaluating standing, courts also consider whether there exists a more directly injured plaintiff to vindicate the public interest. *See Associated Gen. Contractors*, 459 U.S. at 544. "Inferiority" to another plaintiff does not necessitate that we deny standing but it is a relevant factor. *See* 2 Areeda *et al.*, *supra*, § 339, at 332. We are more likely to find no standing if the plaintiff's injury both derives from and is measured by another's more direct injury. *See Adams*, 828 F.2d at 30-31 (existence of superior plaintiffs—employer airline as well as consumers of transatlantic air transportation—militated against employees' standing). Additionally, lack of standing is more likely as layers of superior plaintiffs increase. *See* 2 Areeda *et al.*, *supra*, § 339, at 332.

The district court held that "[t]hose most directly affected by [Andrx's] violation would be the consumers faced to pay artificially high prices for Cardizem." *Andrx Pharm.*, 83F.Supp.2d at 186. It reasoned that "[i]f Andrx's activity violates the antitrust laws, it is because it is keeping others out of the market and thereby maintaining artificially high costs for generic drugs." *Id.* But Biovail's alleged injury is not derived from or measured by the injury to consumers; instead it is measured by the loss of profits it would have otherwise made had it not been excluded from the market. *See Story Parchment*, 282 U.S. at 562-64; *Eastman Kodak Co. v. Southern Photo Co.*, 273 U.S. 359, 378-79, 47 S.Ct.

---

standing "cannot reasonably be restricted to those competitors whom the conspirators hoped to eliminate from the market." *McCready*, 457 U.S. at 479. It thus affirmed the subscribers' standing. Applying the same reasoning, we conclude that Biovail's alleged injury is "so integral an aspect" of the alleged anticompetitive behavior, "there can be no question but that the loss was precisely 'the type of loss that the claimed violations . . . would be likely to cause.'" *Id.* (quoting *Brunswick*, 429 U.S. at 489). When a competitor is excluded from a market by the collusive acts of its rivals, its loss of profits is directly caused by that anticompetitive behavior.

400, 71 L.Ed. 684 (1927). Biovail does not seek damages for profits it would have earned at higher, less competitive prices. *See, e.g., Atlantic Richfield Co. v. USA Petroleum Co.*, 495 U.S. 328, 337, 110 S.Ct. 1884, 109 L.Ed.2d 333 (1990); *Brunswick*, 429 U.S. at 487-89. It seeks damages to compensate for profits it would have earned by competing in the market. Irrespective of consumer injury, an excluded competitor like Biovail suffers a distinct injury if it is prevented from selling its product. "[A] rival has clear standing to challenge the conduct of rival(s) that is illegal precisely because it tends to exclude competitors from the market." 2 Areeda *et al.*, *supra*, § 348, at 387. Unlike the "high probability of substantial overlap" the *Adams* court found between the injury the plaintiffs there alleged (employees' lost jobs and lower wages) and those of more direct victims (company's loss of profits and transatlantic passengers' increased airfare), Biovail's alleged injury is not measured by or derived from consumer plaintiffs. *Adams*, 828 F.2d at 30 n. 12. And to the extent Biovail seeks injunctive relief, its standing is plainly not derivative.

E. *Duplicative Recovery and Complex Apportionment of Damages*

In *Illinois Brick Co. v. Illinois*, 431 U.S. 720, 97 S.Ct. 2061, 52 L.Ed.2d 707 (1977), the Supreme Court held that antitrust suits brought by indirect purchasers increased both the risk of multiple recoveries and the difficulty of apportionment of damages. The Court explained that in addition to adding complexity to the case, apportionment pares the direct purchasers' recovery, thereby diminishing their incentive to bring treble damage actions under section 4 of the Clayton Act. *Id.* at 737-47; *see* McCready, 457 U.S. at 475 n. 11.

The district court concluded that the existence of both consumer suits and Biovail's own suit against HMRI raised "the potential here for duplicative recoveries and inconsistent

holdings." *Id.* As we have explained, however, Biovail's injuries are neither derived from nor measured by injuries consumers may have suffered. Any injury to consumers would result from paying a supracompetitive price for Cardizem CD. Biovail's injury, on the other hand, is the result of foregone profits, i.e., the difference between the competitive market price it would have charged had it been in the market and its total costs. *See Eastman Kodak*, 273 U.S. at 378-79. Moreover, Biovail has settled its suit with HMRI. *See Biovail Corp. Int'l v. Aktiengesellschaft*, Civ. No. 98-1434 (D.N.J. Jan. 31, 2001).[20]

F. Noerr-Pennington Doctrine

Having concluded that dismissal with prejudice was erroneously granted, we must consider Andrx's claim that the Agreement is litigation-related conduct exempted from antitrust liability by the *Noerr-Pennington* doctrine. The *NoerrPennington* doctrine insulates from antitrust challenge competitors' decision to combine to petition the government, even if their underlying intention is to restrain competition or gain advantage over competitors. *See United Mine Workers of Am. v. Pennington*, 381 U.S. 657, 670, 85 S.Ct. 1585, 14 L.Ed.2d 626 (1965); *see also City of Columbia v. Omni Outdoor Adver., Inc.*, 499 U.S. 365, 379-80, 111 S.Ct. 1344, 113 L.Ed.2d 382 (1991) ("The federal antitrust laws also do not regulate the conduct of private individuals in seeking anticompetitive action from the government."). The doctrine is rooted in First Amendment law and "rests ultimately upon a recognition that the antitrust laws, 'tailored as they are for

---

[20] Moreover, the Federal Trade Commission has withdrawn its complaint against HMRI and Andrx and entered into consent agreements with both manufacturers prospectively barring them from entering into certain anticompetitive agreements and requiring that future interim settlements of patent litigation be approved by the court with notice to the Commission. *See* 66 Fed.Reg. 18,636 (proposed consent decree).

the business world, are not at all appropriate for application in the political arena.'" *Omni*, 499 U.S. at 380 (citation omitted).[21]

In *California Motor Transport Co. v. Trucking Unlimited*, the Court extended the right to petition all departments of the government, including the "courts, the third branch of Government." 404 U.S. 508, 510, 92 S.Ct. 609, 30 L.Ed.2d 642 (1972) ("The right of access to the courts is indeed but one aspect of the right of petition."). Whether conduct falls with "[t]he scope of this protection depends, however, on the source, context, and nature of the anticompetitive restraint at issue." *Allied Tube & Conduit Corp. v. Indian Head, Inc.*, 486 U.S. 492, 499, 108 S.Ct. 1931, 100 L.Ed.2d 497 (1988). If anticompetitive harm is caused by the decision of a court, even though granted at the request of a private party, no private restraint of trade occurs because the intervening government action breaks the causal chain. *See* 1 Phillip Areeda & Herbert Hovenkamp, *Antitrust Law* § 202c, at 159-62 (2d ed.2000).

---

[21] The doctrine derives its name from two Supreme Court decisions. The first, *Eastern Railroad Presidents Conference v. Noerr Motor Freight, Inc.*, 365 U.S. 127, 81 S.Ct. 523, 5 L.Ed.2d 464 (1961), held that the antitrust laws do not apply to conduct resulting from valid government actions. The Supreme Court held that attempts by railroads to influence legislation designed to restrict competition from the trucking industry were exempt from antitrust liability. The Court remarked, "no violation of the [Sherman] Act can be predicated upon mere attempts to influence the passage or enforcement of laws." *Id.* at 135. The Court came to the same conclusion in *Pennington*, 381 U.S. 657, 85 S.Ct. 1585, 14 L.Ed.2d 626 (1965). There, mine operators and workers petitioned the Executive Branch to induce the Tennessee Valley Authority to curtail spot market purchases and to increase minimum wages. The Court explained that "[j]oint efforts to influence public officials do not violate the antitrust laws even though intended to eliminate competition. Such conduct is not illegal, either standing alone or as a part of a broader scheme itself violative of the Sherman Act." *Id.* at 670.

Andrx argues that its Agreement should receive the same protection as threatened litigation or an offer of settlement. *See, e.g., Coastal States Mktg., Inc. v. Hunt*, 694 F.2d 1358, 1367 (5th Cir.1983) (extending doctrine to cover activities not necessarily part of petitioning process, but reasonably incident or normally attendant to it, *e.g.*, genuine litigation threat); *McGuire Oil Co. v. Mapco, Inc.*, 958 F.2d 1552, 1560 (11th Cir.1992) (same).[22] We disagree. Although certain litigation conduct is protected under the doctrine, it does not extend to the HMRI-Andrx Agreement. *See California Motor Transp.*, 404 U.S. at 512-13 (examples of unprotected litigation conduct include perjury by witnesses and fraudulently obtained patent); *cf. Omni*, 499 U.S. at 380 ("sham" petitioning such as filing frivolous objections to license application of a competitor to impose expense and delay not protected). In *In re Cardizem CD Antitrust Litigation*, 105 F.Supp.2d 618, the district court found the alleged anticompetitive harm stemming from the Agreement separate from any anticompetitive effects that may have resulted from resolution of the HMRI patent infringement suit. The harm, the court declared, was not the result of a court decision. "Rather, it is the result of purely private conduct and thus constitutes a private restraint of trade subject to liability under the antitrust laws." *Id.* at 635; *see also In re Brand Name Prescription Drugs Antitrust Litig.*, 186 F.3d 781, 789 (7th Cir.1999) ("[T]he doctrine does not authorize anticompetitive *action* in advance of government's adopting the industry's anticompetitive proposal. The doctrine applies when such action is the consequence of

---

[22] *See also* 1 Areeda & Hovenkamp, *supra*, § 205e, at 238 ("Most lawsuits are prefaced by various communications, such as demand letters that expressly or impliedly threaten suit unless the addressee alters its conduct or provides other relief. Such prelitigation communications provide useful notice and facilitate the resolution of controversies. It would be foolish to adopt antitrust rules encouraging suit before communication by penalizing the communication but not the suit.").

legislation or other governmental action, not when it is the means for obtaining such action (or in this case inaction)." (emphasis original)). The Agreement is not unlike a final, private settlement agreement resolving the patent infringement litigation by substituting a market allocation agreement. Such a settlement agreement would not enjoy *Noerr-Pennington* immunity and neither does the Agreement here.

IV. Conclusion

In sum, although the district court correctly dismissed Biovail's antitrust counterclaim for failure to sufficiently allege injury caused by the HMRI-Andrx Agreement, it should have granted the dismissal without prejudice to allow Biovail the opportunity to replead. Accordingly, appeal No. 00-5050 is remanded to the district court for proceedings not inconsistent with this opinion. In light of our holding, we dismiss as moot appeal No. 00-5396.

So ordered.

APPENDIX B

UNITED STATES DISTRICT COURT,
DISTRICT OF COLUMBIA.

No. CIV. A. 98-0099(JPG).

ANDRX PHARMACEUTICALS, INC.,
Plaintiff,

v.

MICHAEL A. FRIEDMAN, LEAD DEPUTY COMMISSIONER, FOOD AND DRUG ADMINISTRATION, *et al.*,
Defendants.

Jan. 6, 2000.

MEMORANDUM

JOHN GARRETT PENN, *District Judge*.

This matter is before the Court on Andrx Pharmaceuticals, Inc.'s Motion to Dismiss Biovail Corporation International's Counterclaim. For the reasons set forth below, the motion will be granted.

I. Background

This case first came before the Court on Andrx Pharmaceuticals, Inc.'s, ("Andrx") motion for a temporary restraining order. Andrx had challenged a Food and Drug Administration ("FDA") regulation that conditioned a period of market exclusivity on the successful defense of a patent infringement action. Andrx sought an order directing the FDA to withdraw its approval of an Abbreviated New Drug Application ("ANDA"), which authorized another company, Mylan Pharmaceuticals, to market a generic version of a drug

that Andrx believed it was entitled to market exclusively for 180 days. This Court granted Andrx's motion for a temporary restraining order, and directed that Mylan Pharmaceuticals cease the marketing, sale, and distribution of the generic drug at issue until the specific date on which Andrx's period of exclusivity was to run. *See* Memorandum filed March 30, 1998. Subsequently, the Court of Appeals for the District of Columbia Circuit ruled in a different case raising the same issue. In that case, *Mova Pharmaceutical Corp. v. Shalala*, 329 U.S.App.D.C. 341, 140 F.3d 1060 (1998), the court invalidated the FDA regulation conditioning the 180-day period of exclusivity on the requirement that the first ANDA applicant successfully defend a patent infringement suit. In light of this Court's opinion, and that of the Court of Appeals in *Mova,* the government has conceded this issue, and the FDA has since issued new guidelines. *See* Federal Defendants' Reply to Plaintiff's Opposition to Its Motion to Dismiss [# 30]; Andrx's Statement in Support of Motion to Dismiss at 1-2. Moreover, Andrx has voluntarily dismissed its complaint against the FDA and Faulding, Inc. *See* Notice of Dismissal as to Michael A. Friedman [# 39]; Notice of Dismissal as to Faulding, Inc. [# 44]. Thus, the only remaining issues before the Court are those raised by defendant/counterclaim-plaintiff Biovail Corporation International ("Biovail").

As did the original issue before the Court, the pending matter relates to statutory and regulatory provisions governing the generic pharmaceutical industry. Only the relevant provisions will be discussed here.[1] Specifically at issue here are certain provisions among those enacted by the Hatch-Waxman Amendments in 1984, which sought to

---

[1] For a more thorough discussion of the statutory and regulatory provisions governing the marketing of generic drugs, see the Court of Appeals' discussion in *Mova Pharmaceutical Corp. v. Shalala*, 329 U.S.App.D.C. 341, 344-46, 140 F.3d 1060, 1063-65 (1998).

simplify the procedure for FDA approval of generic drugs and to promote the public interest in the availability of such drugs. Pursuant to the Hatch-Waxman Amendments, the original applicant for FDA approval of a drug must, as had previously been required, complete a New Drug Application ("NDA"), which must include information documenting the drug's safety and effectiveness. *See Mova Pharmaceutical*, 329 U.S.App.D.C. at 344, 140 F.3d at 1063. Subsequent applicants who wish to market generic versions of the pioneer drug may file an Abbreviated New Drug Application ("ANDA"), which may rely on the safety assessments of the pioneer drug. *See id.* Among the requirements for an ANDA is that the applicant must certify that the proposed generic drug will not infringe on any patents applicable to the pioneer drug. There are four possible certifications, one of which (the so-called paragraph IV certification) certifies that the patent related to the pioneer drug "is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted." 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

When an ANDA applicant makes a paragraph IV certification, the patent-holder has forty-five days within which to bring a patent infringement suit against the applicant. If the patent-holder brings such a suit, the FDA's approval of the ANDA automatically is delayed for thirty months, a period which may be extended or shortened by the court. 21 U.S.C. § 355(j)(5)(B)(iii).

The provision of the Hatch-Waxman amendments which occasioned the original claims in this case, and which is at the heart of the antitrust allegations in the counterclaims, is a provision that specifies how subsequent ANDA applications are to be treated; specifically, it is a provision which provides

that subsequent ANDA applications may not be made effective until one of two trigger dates:

> If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing [sic] such a certification, the application shall be made effective not earlier than one hundred and eighty days after—
>
> (I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or
>
> (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.

21 U.S.C. § 355(j)(5)(B)(iv). This provision effectively permits a 180- day period of market exclusivity for the first ANDA applicant within which the applicant may market its generic drug without competition from subsequent ANDA applicants. It ensures that any subsequent ANDA applicant may not market its generic version of the pioneer drug until 180 days from the earlier of either (1) the first commercial marketing by the first ANDA applicant, or (2) a court decision in a patent infringement suit (one brought pursuant to the statute within 45 days of the first ANDA application) finding the patent to be invalid or not infringed. This provision is intended to reward the first ANDA applicant for incurring the risks of being the first on the market with a generic version of a pioneer drug. *See, e.g., Mova*, 329 U.S.App. D.C. at 356, 140 F.3d at 1075.

Andrx originated this action challenging FDA's practice of approving in certain cases subsequent ANDAs prior to the running of the 180-day period of exclusivity to which the primary ANDA applicant was entitled. Of immediate concern

to Andrx was FDA's approval of an ANDA submitted by Mylan Pharmaceuticals for a generic version of Dilacor XR®. This Court granted a temporary restraining order and directed Mylan Pharmaceuticals to cease the marketing, sale, and distribution of its generic version of Dilacor XR® UNTIL the date on which Andrx's statutory period of exclusivity was to run. *See* Memorandum and Order, March 30, 1998. Subsequently, in another case, the D.C. Circuit invalidated the FDA regulation under which the agency approved Mylan Pharmaceuticals' ANDA, as well as others in similar situations, prior to the first ANDA applicant's enjoyment of the 180-day period of exclusivity. *See Mova*, 329 U.S.App. D.C. at 357, 140 F.3d at 1076 (affirming district court's decision striking down the "successful defense" requirement).

Biovail now has filed a counterclaim against Andrx, alleging antitrust violations. Biovail alleges that Andrx colluded with Hoechst Marion Roussel, Inc. ("HMRI") to delay the implementation of the 180-day period of market exclusivity, intending to restrain trade in less expensive generic drugs and nearly achieving a monopoly, in violation of Sections 1 and 2 of the Sherman Act. Biovail also alleges the common law violations of unfair competition, tortious interference with prospective advantage, and tortious interference with contact.

BIOVAIL'S COUNTERCLAIM

Andrx was the first to seek an ANDA for approval of a generic version of Cardizem® CD ("Cardizem"), a diltiazem-based drug [2] taken for the treatment of hypertension and angina. Biovail's Counterclaim §§ 10, 11. Cardizem is

---

[2] Diltiazem is a drug that "blocks the movement of calcium particles into the cells of the heart and blood vessels," thus increasing the flow of blood through the heart and thereby lowering blood pressure. Counterclaim § 24.

manufactured and marketed by HMRI.[3] Counterclaim § 12. Within the time set forth by the statute, HMRI and others sued Andrx in the U.S. District Court for the Southern District of Florida, alleging patent infringement. Counterclaim § 16. In the meantime, in September 1997, the FDA gave tentative approval to Andrx's ANDA. Counterclaim § 17. That tentative approval would become effective, under the statute, either upon the expiration of the 30-month waiting period, or the date of a court decision in Andrx's favor, whichever came first. Counterclaim § 17.

Biovail alleges that in September 1997, HMRI and Andrx entered into an agreement under which HMRI would make non-refundable payments to Andrx, in consideration of which Andrx agreed not to introduce its generic version of Cardizem when the 30-month period expired. Counterclaim § 18. These quarterly payments of $10,000,000 allegedly began on July 3, 1998, the date on which the 30-month stay imposed by the statute would expire and Andrx would therefore be permitted by the FDA to introduce its generic version into commerce, and are to continue until the Florida patent case is finally concluded or certain other events occur. *Id.* Biovail alleges that this agreement was entered into for the purpose of thwarting congressional intent and with the intent to prevent generic versions of Cardizem from entering the market within the time they would otherwise do so under the Act. Counterclaim § 19. The consequence of the agreement, according to Biovail's allegations, is to prolong HMRI's ability to charge artificially high prices for Cardizem and thereby to continue to reap the benefits of a substantial monopoly. Andrx benefits as a consequence of this agreement

---

[3] According to Biovail's counterclaim, Cardem Capital L.P. ("Cardem") holds the approved NDA for Cardizem and is the assignee of three related patents for Cardizem CD. It is Biovail's understanding that Cardem holds these patents for the benefit of, or has assigned the rights under the patents to, HMRI. Counterclaim § 12.

by being paid $40,000,000 per year by HMRI while not having to place its drug into competition with other generic drugs. Counterclaim § 22.

Biovail's Cardizem Product

Biovail began its development of diltiazem-based products in 1993, when it entered into a joint-development agreement with Hoechst-Roussel Pharmaceuticals, Inc. ("HRPI"), a subsidiary of Hoechst Aktiengesellschaft ("Hoechst"). Counterclaim § 31. The purpose of this agreement was to develop and market diltiazem-based drugs that would compete directly with Cardizem, then being sold by Marion Merrell Dow, Inc. ("MMD"). Counterclaim § 31. The first product produced pursuant to this agreement was a once-daily form to be sold under the name Tiazac®. HRPI, relying on Biovail's expertise and technology, compiled and filed a NDA for Tiazac, which was approved by the FDA in September 1995. Counterclaim § 32. MMD sued, alleging Tiazac infringed certain patents licensed by MMD from another company, Elan p.l.c. ("Elan"). Counterclaim § 33. HRPI defended the action on its own behalf and on behalf of Biovail. *Id.*

During the pendency of MMD's patent infringement action, Hoechst acquired MMD and merged it into HRPI, creating HMRI. Counterclaim § 34. According to Biovail, this merger effectively breached the development agreement between it and HRPI. *Id.*

Biovail sued MMD, and its affiliate Carderm, while the acquisition was pending. Counterclaim § 35. That action resulted in a settlement agreement pursuant to which "Hoechst, HRPI, MMD, and Carderm agreed that they and their successors and assigns would not, at any future time, initiate any regulatory proceedings or legal actions that would interfere with Biovail's pursuit of regulatory approvals of its

once-daily, extended-release diltiazem products that were and would be developed." Counterclaim § 35.[4]

Biovail's ANDA for its Generic Version of Cardizem

Biovail submitted an ANDA with a subclass IV certification to FDA for its generic form of Cardizem. Counterclaim § 41. On June 19, 1997, Biovail gave the required notice to those with NDA and patent rights related to Cardizem. *Id.* No patent infringement suit related to Biovail's generic version of Cardizem has ever been filed against Biovail. Counterclaim § 42. However, in August 1997, HMRI attempted, unsuccessfully, to convince Biovail to agree to an agreement under which Biovail would postpone marketing its generic. Counterclaim § 43. Subsequently, in September 1997, Andrx announced that it had entered into such an agreement with HMRI under which Andrx would postpone marketing its generic version of Cardizem. Counterclaim § 44.

Biovail's Damages

Biovail alleges in excess of $1 billion in damages. Counterclaim § 55. These damages allegedly include "unnecessary and artificial costs and delay in sales due to Andrx's interference with Biovail's rights; injury to Biovail's reputation, good will, and present value, as well as to Biovail's prospective advantage." *Id.*

II. Discussion

Andrx moves pursuant to *Federal Rule of Civil Procedure* 12(b)(6) to dismiss Biovail's counterclaim for failing to state a claim upon which relief may be granted, on the grounds that

---

[4] In December 1995, the Federal Trade Commission ("FTC"), as a condition for its not challenging the MMD-HPRI merger, issued an order under which Biovail was granted rights that would allow it to market Tiazac and aid Biovail in its pursuit of FDA approval for extended release products. Counterclaim § 36.

Biovail lacks standing to assert the alleged antitrust violations. Andrx also seeks dismissal of the remaining claims because they lack an independent basis for federal jurisdiction, as well as on the merits.

In order to recover for alleged violations of the antitrust laws, Biovail must establish that it has "antitrust standing," that is, it must establish that it has suffered injury by reason of action forbidden by the antitrust laws. *See* 15 U.S.C. § 15; *Indium Corp. v. Semi-Alloys, Inc.*, 781 F.2d 879, 882 (Fed.Cir.1985). In *Associated Gen. Contractors v. California State Council of Carpenters*, 459 U.S. 519, 534-545, 103 S.Ct. 897, 74 L.Ed.2d 723 (1983), the Supreme Court set out a number of factors courts should consider in determining whether a plaintiff has antitrust standing. These factors include: whether there is a causal connection between the alleged injury and the antitrust violation; whether the nature of the injury is of the type the antitrust laws were meant to prevent (the "antitrust injury" requirement); the directness or indirectness of the injury; the existence of more direct victims of the alleged violation; the speculative nature of the harm; and the potential for duplicative recoveries. *See id.; Indium*, 781 F.2d at 882; *City of Pittsburgh v. West Penn Power Co.*, 147 F.3d 256, 264 (3d Cir.1998) (listing the *Associated General* factors and characterizing them as a "the passageway through which antitrust plaintiffs must advance"). A careful consideration of these factors leads the Court to conclude that Biovail has not established the existence of antitrust standing.

1. *Causal Connection and the Existence of "Antitrust Injury"*

The existence of "antitrust injury" is essential to establish standing. *See, e.g., Atlantic Richfield Co. v. USA Petroleum Co.*, 495 U.S. 328, 334, 110 S.Ct. 1884, 109 L.Ed.2d 333 (1990); *West Penn Power*, 147 F.3d at 265 (stating that "[i]f

antitrust injury is not found, further inquiry is unnecessary"). Antitrust injury is "injury of the type the antitrust laws were intended to prevent and that flows from that which makes defendants' acts unlawful." *Brunswick Corp. v. Pueblo Bowl-O-Mat, Inc.*, 429 U.S. 477, 489, 97 S.Ct. 690, 697, 50 L.Ed.2d 701 (1977). It is not sufficient merely to establish a causal connection; rather, the alleged antitrust injury must be *caused by* the alleged antitrust violation; a direct link must be established. *See Brunswick*, 429 U.S. at 489, 97 S.Ct. at 697 (stating that antitrust plaintiffs "must prove more than injury causally linked to an illegal presence in the market"); *West Penn Power*, 147 F.3d at 268.

Biovail fails to establish the requisite causal connection. At the time of the briefing of these motions, the FDA had not yet approved Biovail's pending ANDA relating to its generic version of Cardizem. In recent supplemental briefing, the parties have not otherwise informed the Court. Thus, even if Andrx and HMRI had not entered into the challenged agreement, Biovail would not at this time be able lawfully to market its generic version of Cardizem. Any loss in potential sales of Biovail's product, therefore, is only marginally, if at all, related to the agreement. Also, even if this Court were to invalidate the Andrx-HMRI agreement, there is no requirement that Andrx proceed to market at this time. Andrx is free to wait until the conclusion of the Florida litigation before it begins to market its generic, and indeed the statute contemplates that possibility. Under those circumstances, no generic Cardizem manufacturer could market its product until 180 days from the conclusion of the litigation, an eventuality perfectly within the scheme set forth by the Hatch-Waxman Amendments. At least some of the potential delay in the marketing of generic versions of Cardizem, then, is more

directly caused by the statutory scheme than by any agreement between Andrx and HMRI.[5]

Biovail insists that it has suffered "antitrust injury", stating that "[t]he Sherman Act specifically prohibits agreements that restrain overall competition, which is what the facts show the HMRI-Andrx competition-delaying agreement to be." Biovail's Opposition at 30. This is only one part of the equation, however. Even if the Court were to determine that Andrx's actions violated the antitrust laws, this does not end the inquiry into whether *Biovail* has suffered "antitrust injury", as that concept has been defined. Biovail alleges "unnecessary and artificial costs and delay in sales" as well as "damages to [its] prospective advantage" because of its inability to compete. However, Biovail's allegations that it has been unable to compete in the generic Cardizem market does not flow from the allegedly unlawful agreement between Andrx and HMRI. The reason Biovail cannot enter the market is because of the existence of a troublesome statutory scheme that prohibits it from marketing a drug until the first ANDA recipient goes to market, and which places no restrictions on when, or even whether, that applicant must go to market. Indeed, Biovail has not even obtained the regulatory approval to proceed to market, thus it is barred from selling its generic

---

[5] It is worth noting that in *Mova*, the Court of Appeals referred to the Andrx-HMRI agreement when it considered the consequences of following a literal reading of the Hatch-Waxman Amendments. The Court stated the potentiality that "the first applicant could even collude with the original patent-holder to prolong their litigation, and thereby keep the second applicant's drug off the market indefinitely." *Move*, 329 U.S.App.D.C. at 353, 140 F.3d at 1072. In a footnote, the Court cited the example offered by Biovail, which filed an amicus brief in the Court of Appeals in that case. *Id.* 329 U.S.App.D.C. at 353 n. 14, 140 F.3d at 1072 n. 14. Nevertheless, the court concluded that "we are not persuaded that this third anomaly suffices to show that a literal reading of the statute leads to results manifestly inconsistent with the intent of Congress". *Id.* 329 U.S.App.D.C. at 353, 140 F.3d at 1072.

drug irrespective of the Andrx-HMRI agreement. Under these circumstances, the Court cannot find that Biovail can establish that it has suffered "antitrust injury". *Cf. West Penn Power*, 147 F.3d at 268 ("Here, the interposition of the regulatory scheme and actions of the parties . . . interferes with the chain of causation. The statutory scheme precluded competition without the requisite regulatory permission. As Professors Areeda & Hovenkamp describe, 'a plaintiff cannot be injured in fact by private conduct excluding him from the market when a statute prevents him from entering that market in any event.'") (citation omitted).

The existence of alternative trigger dates under that statute further supports a finding that Biovail's alleged injury does not flow directly from Andrx's alleged antitrust violation. The statute's second triggering date is the completion of the patent litigation--thus, the statute does provide a time at which subsequent generic competitors may proceed to market, even if the first ANDA applicant never does so. That is, 180 days from the completion of the antitrust litigation, other generics, *which have themselves received FDA approval* in the form of approved ANDAs, may proceed to market notwithstanding the action or inaction of the first ANDA applicant.

Biovail also alleges that its reputation and present value, as measured by its stock value and other criteria, have been injured by the agreement. Even if this could be proven, however, injury to Biovail's reputation is not the type of injury sought to be redressed by the antitrust laws and thus cannot provide the basis to establish antitrust standing. *Cf. Brunswick*, 429 U.S. at 488, 97 S.Ct. 697 (stating that the antitrust laws "were enacted for 'the protection of competition, not competitors'") (citation omitted).

Biovail also attempts to establish standing by asserting a right "to require compliance with those statutory provisions [contained in the Hatch-Waxman Amendments and the

Sherman Act] and to prevent its protected interest from being damaged." Opposition at 28. For this proposition, Biovail cites *Bristol-Myers Squibb Co. v. Shalala*, 320 U.S.App. D.C. 32, 36, 91 F.3d 1493, 1497 (1996), which states that where "a statutory provision reflects a legislative purpose to protect a competitive interest, the protected competitor has standing to require compliance with that provision." First, that case is not an antitrust case, and nothing in that case suggests that this Court should abandon the well-developed antitrust standing inquiry. In any event, the *Bristol-Myers* inquiry does not help Biovail's attempt to establish standing. Here, the statutory provisions with which Biovail presumably seeks compliance have dual and perhaps at times competing interests—that of fostering generic drug production and marketing, as well as protecting the first ANDA applicant and in particular, one which has been sued for patent infringement by the pioneer drug's manufacturer. Moreover, it is not clear what kind of "compliance" Biovail seeks: complying with the provisions of the Hatch-Waxman amendments would not require Andrx to proceed immediately to market. Again, this demonstrates that Biovail's asserted injury, although perhaps tied to the alleged wrongdoing by Andrx, does not "flow from" that wrongdoing.

2. *Speculative Nature of the Harm*

The speculative nature of the harm is among the factors the Court is to consider in determining whether Biovail has sufficiently established the existence of antitrust standing. *See, e.g., Indium*, 781 F.2d at 882. The primary injury alleged here by Biovail—delay in sales—is speculative because there is no evidence that absent the Andrx-HMRI agreement, Biovail would be marketing its generic drug. There is the possibility that Andrx would not have gone to market even absent the agreement with HMRI, and certainly the Hatch-Waxman amendments would permit and protect that delay until the conclusion of the patent litigation. Even if there is a

question of fact regarding *whether* Andrx would have proceeded to market notwithstanding the agreement, there is no indication *when* Andrx might have done so. Most importantly, damages are speculative because *even today*, Biovail *could not go to market with a generic version of Cardizem*, because it has not received FDA approval. *Cf. West Penn Power*, 147 F.3d at 268 (finding the alleged injury to be speculative where it would be difficult to measure and "because the injury claimed may never occur"); *see also Associated General*, 459 U.S. at 542, 103 S.Ct. at 911 (noting damages were "highly speculative" where the effects were indirect and may have been produced by independent factors). The Andrx-HMRI agreement, even if potentially an impediment to Biovail's entry into the relevant generic market, is not the only such impediment, and not the most direct.

3. *Potential for Duplicative Recoveries*

In determining whether a party has antitrust standing, one of the concerns is whether the that party is a proper party to bring a private antitrust action. *See Associated General*, 459 U.S. at 535 n. 31, 103 S.Ct. at 907 n. 31. The Court must ask whether there exist more direct victims of the alleged antitrust violations, and whether there is a potential for duplicative recovery or complex apportionment of damages. *See Id.* at 544, 103 S.Ct. at 911; *West Penn Power*, 147 F.3d at 264; *Indium*, 781 F.2d at 882. This factor also causes the Court concern in this case. First, there clearly are other, more direct victims of Andrx's alleged violation. If Andrx's activity violates the antitrust laws, it is because it is keeping others out of the market and thereby maintaining artificially high costs for generic drugs. *See, e.g.*, Biovail's Opp. at 12-13. Those most directly affected by such a violation would be the consumers forced to pay artificially high prices for Cardizem. Also more directly affected than Biovail would be any potential competitor that has obtained FDA approval and thus

would be ready and able to enter the generic market as soon as any period of exclusivity for Andrx expired.

There also is the potential here for duplicative recoveries and inconsistent holdings. Biovail currently is proceeding in another district against HMRI and others alleging various antitrust and other allegations. *See Biovail Corp. v. Hoechst Aktiengesellschaft*, 49 F.Supp.2d 750 (D.N.J.1999). Among the facts in support of the alleged violations, Biovail has offered the Andrx-HMRI agreement. *See id.* at 766. Only recently, that court denied a motion to dismiss. Thus, Biovail stands to recover, potentially, for alleged antitrust violations arising, in part, from the agreement that is the subject of the counterclaims now before this Court.

Also, there is currently pending before a Multi-District Litigation Panel numerous actions alleging various federal and state antitrust injuries relating to the very agreement now challenged in this Court. *See* MDL 1278, In re: Cardizem CD Antitrust Litigation, Transfer Order, June 11, 1999 (stating that "the Panel finds that the actions in this litigation involve common question of fact concerning allegations that Andrx and HMRI violated various state or federal antitrust and other statutory and common laws in connection with the sale of Cardizem Cd").

III. Conclusion

For the reasons set forth in this memorandum, the Court concludes that Biovail lacks standing to bring the asserted antitrust violations. The Court further will dismiss, without prejudice, the remaining claims for lack of jurisdiction. An appropriate order accompanies this memorandum.

APPENDIX C

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

[Filed Sept 14, 2001]

No. 00-5050
September Term, 2001
98cv00099

ANDRX PHARMACEUTICALS, INC.,
Appellee,

v.

BIOVAIL CORPORATION INTERNATIONAL,
Appellant.

Consolidated with 00-5396

BEFORE: Ginsburg, *Chief Judge*; Edwards, Williams, Sentelle, Henderson, Randolph, Rogers, Tatel and Garland, *Circuit Judges*

ORDER

Upon consideration of appellee's petition for rehearing en banc, and the absence of a request by any member of the court for a vote, it is

ORDERED that the petition be denied.

Per Curiam

FOR THE COURT:
Mark J. Langer, Clerk

/s/ Nancy G. Dunn
NANCY G. DUNN
Deputy Clerk

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

[Filed Sept 14, 2001]

No. 00-5050
September Term, 2001
98cv00099

ANDRX PHARMACEUTICALS, INC.,
Appellee,

v.

BIOVALL CORPORATION INTERNATIONAL,
Appellant.

Consolidated with 00-5396

BEFORE: Henderson, Randolph and Garland, *Circuit Judges*

ORDER

Upon consideration of appellee's petition for rehearing filed August 29, 2001, it is

ORDERED that the petition be denied.

Per Curiam

FOR THE COURT:
Mark J. Langer, Clerk

/s/ Nancy G. Dunn
NANCY G. DUNN
Deputy Clerk

APPENDIX D

21 U.S.C. § 355(j)(2) & (5)

§ 355. New drugs

(j) Abbreviated new drug applications

(2)(A) An abbreviated application for a new drug shall contain—

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is

required to be filed under subsection (b) or (c) of this section—

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B)(i) An applicant who makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give the notice required by clause (ii) to—

(I) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(II) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(ii) The notice referred to in clause (i) shall state that an application, which contains data from bioavailability or bioequivalence studies, has been submitted under this

subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(iii) If an application is amended to include a certification described in subparagraph (A)(vii)(IV), the notice required by clause (ii) shall be given when the amended application is submitted.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds—

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

* * *

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined under the following:

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,

(II) if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of Title 35, or

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of Title 28, for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(iv) If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after—

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.

(C) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether

such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii).

The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section for such drug.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

35 U.S.C. § 271

§ 271. Infringement of patent

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

(b) Whoever actively induces infringement of a patent shall be liable as an infringer.

(c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.

(d) No patent owner otherwise entitled to relief for infringement or contributory infringement of a patent shall be

denied relief or deemed guilty of misuse or illegal extension of the patent right by reason of his having done one or more of the following:

(1) derived revenue from acts which if performed by another without his consent would constitute contributory infringement of the patent;

(2) licensed or authorized another to perform acts which if performed without his consent would constitute contributory infringement of the patent;

(3) sought to enforce his patent rights against infringement or contributory infringement;

(4) refused to license or use any rights to the patent; or

(5) conditioned the license of any rights to the patent or the sale of the patented product on the acquisition of a license to rights in another patent or purchase of a separate product, unless, in view of the circumstances, the patent owner has market power in the relevant market for the patent or patented product on which the license or sale is conditioned.

(e)(1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

(2) It shall be an act of infringement to submit—

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section

505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent, or

(B) an application under section 512 of such Act or under the Act of March 4, 1913 (21 U.S.C. 151-158) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques and which is claimed in a patent or the use of which is claimed in a patent,

if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug or veterinary biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

(3) In any action for patent infringement brought under this section, no injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention under paragraph (1).

(4) For an act of infringement described in paragraph (2)—

(A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed,

(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug or veterinary biological product, and

(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United

States or importation into the United States of an approved drug or veterinary biological product.

The remedies prescribed by subparagraphs (A), (B), and (C) are the only remedies which may be granted by a court for an act of infringement described in paragraph (2), except that a court may award attorney fees under section 285.

(f)(1) Whoever without authority supplies or causes to be supplied in or from the United States all or a substantial portion of the components of a patented invention, where such components are uncombined in whole or in part, in such manner as to actively induce the combination of such components outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(2) Whoever without authority supplies or causes to be supplied in or from the United States any component of a patented invention that is especially made or especially adapted for use in the invention and not a staple article or commodity of commerce suitable for substantial noninfringing use, where such component is uncombined in whole or in part, knowing that such component is so made or adapted and intending that such component will be combined outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent. In an action for infringement of a process patent, no remedy may be granted for infringement on account of the noncommercial use or retail sale of a product unless there is no adequate remedy under this title for

infringement on account of the importation or other use, offer to sell, or sale of that product. A product which is made by a patented process will, for purposes of this title, not be considered to be so made afte—

(1) it is materially changed by subsequent processes; or

(2) it becomes a trivial and nonessential component of another product.

(h) As used in this section, the term "whoever" includes any State, any instrumentality of a State, and any officer or employee of a State or instrumentality of a State acting in his official capacity. Any State, and any such instrumentality, officer, or employee, shall be subject to the provisions of this title in the same manner and to the same extent as any nongovernmental entity.

(i) As used in this section, an "offer for sale" or an "offer to sell" by a person other than the patentee, or any designee of the patentee, is that in which the sale will occur before the expiration of the term of the patent.

35 U.S.C. § 282

§ 282. Presumption of validity; defenses

A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. Notwithstanding the preceding sentence, if a claim to a composition of matter is held invalid and that claim was the basis of a determination of nonobviousness under section 103(b)(1), the process shall no longer be considered nonobvious solely on the basis of section 103(b)(1). The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.

The following shall be defenses in any action involving the validity or infringement of a patent and shall be pleaded:

(1) Noninfringement, absence of liability for infringement or unenforceability,

(2) Invalidity of the patent or any claim in suit on any ground specified in part II of this title as a condition for patentability,

(3) Invalidity of the patent or any claim in suit for failure to comply with any requirement of sections 112 or 251 of this title,

(4) Any other fact or act made a defense by this title.

In actions involving the validity or infringement of a patent the party asserting invalidity or noninfringement shall give notice in the pleadings or otherwise in writing to the adverse party at least thirty days before the trial, of the country, number, date, and name of the patentee of any patent, the title, date, and page numbers of any publication to be relied upon as anticipation of the patent in suit or, except in actions in the United States Claims Court, as showing the state of the art, and the name and address of any person who may be relied upon as the prior inventor or as having prior knowledge of or as having previously used or offered for sale the invention of the patent in suit. In the absence of such notice proof of the said matters may not be made at the trial except on such terms as the court requires. Invalidity of the extension of a patent term or any portion thereof under section 154(b) or 156 of this title because of the material failure—

(1) by the applicant for the extension, or

(2) by the Director,to comply with the requirements of such section shall be a defense in any action involving the infringement of a patent during the period of the extension of

its term and shall be pleaded. A due diligence determination under section 156(d)(2) is not subject to review in such an action.

35 U.S.C. § 284

§ 284. Damages

Upon finding for the claimant the court shall award the claimant damages adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use made of the invention by the infringer, together with interest and costs as fixed by the court.

When the damages are not found by a jury, the court shall assess them. In either event the court may increase the damages up to three times the amount found or assessed. Increased damages under this paragraph shall not apply to provisional rights under section 154(d) of this title.

The court may receive expert testimony as an aid to the determination of damages or of what royalty would be reasonable under the circumstances.

APPENDIX E

CODE OF FEDERAL REGULATIONS (1997)
TITLE 21—FOOD AND DRUGS

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCHAPTER D—DRUGS FOR HUMAN USE
PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG OR AN ANTIBIOTIC DRUG SUBPART D—FDA ACTION ON APPLICATIONS AND ABBREVIATED APPLICATIONS

---

§ 314.107 Effective date of approval of a 505(b)(2) application or abbreviated new drug application under section 505(j) of the act.

(a) General. A drug product may be introduced or delivered for introduction into interstate commerce when approval of the application or abbreviated application for the drug product becomes effective. Except as provided in this section, approval of an application or abbreviated application for a drug product becomes effective on the date FDA issues an approval letter under § 314.105 for the application or abbreviated application.

(b) Effect of patent on the listed drug. If approval of an abbreviated new drug application submitted under section 505(j) of the act or of a 505(b)(2) application is granted, that approval will become effective in accordance with the following:

(1) Date of approval letter. Except as provided in paragraphs (b)(3), (b)(4), and (c) of this section, approval will become effective on the date FDA issues an approval letter under § 314.105 if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that:

(i) There are no relevant patents; or

(ii) The applicant is aware of a relevant patent but the patent information required under section 505 (b) or (c) of the act has not been submitted to FDA; or

(iii) The relevant patent has expired; or

(iv) The relevant patent is invalid, unenforceable, or will not be infringed.

(2) Patent expiration. If the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent will expire on a specified date, approval will become effective on the specified date.

(3) Disposition of patent litigation.

(i)(A) Except as provided in paragraphs (b)(3)(ii), (b)(3)(iii), and (b)(3)(iv) of this section, if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent is invalid, unenforceable, or will not be infringed, and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement within 45 days of receipt by the patent owner of the notice of certification from the applicant under § 314.52 or § 314.95, approval may be made effective 30 months after the date of the receipt of the notice of certification by the patent owner or by the exclusive licensee (or their representatives) unless the court has extended or reduced the period because of a failure of either the plaintiff or defendant to cooperate reasonably in expediting the action; or

(B) If the patented drug product qualifies for 5 years of exclusive marketing under § 314.108(b)(2) and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement during the 1-year period beginning 4 years after the date the patented drug was approved and within 45 days of receipt by the patent owner of the notice of certification, the approval may be made

effective at the expiration of the 7 1/2 years from the date of approval of the application for the patented drug product.

(ii) If before the expiration of the 30-month period, or 7 1/2 years where applicable, the court issues a final order that the patent is invalid, unenforceable, or not infringed, approval may be made effective on the date the court enters judgment;

(iii) If before the expiration of the 30-month period, or 7 1/2 years where applicable, the court issues a final order or judgment that the patent has been infringed, approval may be made effective on the date the court determines that the patent will expire or otherwise orders; or

(iv) If before the expiration of the 30-month period, or 7 1/2 years where applicable, the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug product until the court decides the issues of patent validity and infringement, and if the court later decides that the patent is invalid, unenforceable, or not infringed, approval may be made effective on the date the court enters a final order or judgment that the patent is invalid, unenforceable, or not infringed.

(v) In order for an approval to be made effective under paragraph (b)(3) of this section, the applicant must receive an approval letter from the agency indicating that the application has received final approval. Tentative approval of an application does not constitute "approval" of an application and cannot, absent a final approval letter from the agency, result in an effective approval under paragraph (b)(3) of this section.

(4) Multiple certifications. If the applicant has submitted certifications under § 314.50(i) or § 314.94(a)(12) for more than one patent, the date of approval will be calculated for each certification, and the approval will become effective on the last applicable date.

(c) Subsequent abbreviated new drug application submission.

(1) If an abbreviated new drug application contains a certification that a relevant patent is invalid, unenforceable, or will not be infringed and the application is for a generic copy of the same listed drug for which one or more substantially complete abbreviated new drug applications were previously submitted containing a certification that the same patent was invalid, unenforceable, or would not be infringed and the applicant submitting the first application has successfully defended against a suit for patent infringement brought within 45 days of the patent owner's receipt of notice submitted under § 314.95, approval of the subsequent abbreviated new drug application will be made effective no sooner than 180 days from whichever of the following dates is earlier:

(i) The date the applicant submitting the first application first commences commercial marketing of its drug product; or

(ii) The date of a decision of the court holding the relevant patent invalid, unenforceable, or not infringed.

(2) For purposes of paragraph (c)(1) of this section, the "applicant submitting the first application" is the applicant that submits an application that is both substantially complete and contains a certification that the patent was invalid, unenforceable, or not infringed prior to the submission of any other application for the same listed drug that is both substantially complete and contains the same certification. A "substantially complete" application must contain the results of any required bioequivalence studies, or, if applicable, a request for a waiver of such studies.

(3) For purposes of paragraph (c)(1) of this section, if FDA concludes that the applicant submitting the first application is not actively pursuing approval of its abbre-

viated application, FDA will make the approval of subsequent abbreviated applications immediately effective if they are otherwise eligible for an immediately effective approval.

(4) For purposes of paragraph (c)(1)(i) of this section, the applicant submitting the first application shall, if sued for patent infringement, notify FDA of the date that it commences commercial marketing of its drug product. Commercial marketing commences with the first date of introduction or delivery for introduction into interstate commerce outside the control of the manufacturer of a drug product, except for investigational use under part 312 of this chapter, but does not include transfer of the drug product for reasons other than sale within the control of the manufacturer or application holder. If an applicant does not promptly notify FDA of such date, the effective date of approval shall be deemed to be the date of the commencement of first commercial marketing.

(d) Delay due to exclusivity. The agency will also delay the effective date of the approval of an abbreviated new drug application under section 505(j) of the act or a 505(b)(2) application if delay is required by the exclusivity provisions in § 314.108. When the effective date of an application is delayed under both this section and § 314.108, the effective date will be the later of the 2 days specified under this section and § 314.108.

(e) Court actions.

(1) References to actions of "the court" in paragraphs (b) and (c) of this section are to the court that enters final judgment from which no appeal can be or has been taken.

(2) For purposes of establishing the effective date of approval based on a court judgment, the following dates shall be deemed to be the date of the final decision of the court on the patent issues:

(i) If the district court enters a decision that the patent is invalid, unenforceable, or not infringed, and the decision is not appealed, the date on which the right to appeal lapses.

(ii) If the district court enters a decision that the patent is invalid, unenforceable, or not infringed, and the decision is appealed, the date of the first decision or order by a higher court holding or affirming the decision of the district court that the patent is invalid, unenforceable, or not infringed.

(iii) If the district court enters a decision that the patent is infringed, and the decision is appealed, the date on which the district court enters a judgment that the patent is invalid, unenforceable, or not infringed pursuant to a mandate issued by a court of appeals.

(iv) The applicant shall submit a copy of the entry of the order or judgment to the Office of Generic Drugs (HFD-600), or to the appropriate division in the Office of Drug Evaluation I (HFD-100) or Office of Drug Evaluation II (HFD- 500), whichever is applicable, within 10 working days of a final judgment.

(f) Computation of 45-day time clock.

(1) The 45-day clock described in paragraph (b)(3) of this section begins on the day after the date of receipt of the applicant's notice of certification by the patent owner or its representative, and by the approved application holder. When the 45th day falls on Saturday, Sunday, or a Federal holiday, the 45th day will be the next day that is not a Saturday, Sunday, or a Federal holiday.

(2) The abbreviated new drug applicant or the 505(b)(2) applicant shall notify FDA immediately of the filing of any legal action filed within 45 days of receipt of the notice of certification. If the applicant submitting the

abbreviated new drug application or the 505(b)(2) application or patent owner or its representative does not notify FDA in writing before the expiration of the 45-day time period or the completion of the agency's review of the application, whichever occurs later, that a legal action for patent infringement was filed within 45 days of receipt of the notice of certification, approval of the abbreviated new drug application or the 505(b)(2) application will be made effective immediately upon expiration of the 45 days or upon completion of the agency's review and approval of the application, whichever is later. The notification to FDA of the legal action shall include:

(i) The abbreviated new drug application or 505(b)(2) application number.

(ii) The name of the abbreviated new drug or 505(b)(2) application applicant.

(iii) The established name of the drug product or, if no established name exists, the name(s) of the active ingredient(s), the drug product's strength, and dosage form.

(iv) A certification that an action for patent infringement identified by number, has been filed in an appropriate court on a specified date.

The applicant of an abbreviated new drug application shall send the notification to FDA's Office of Generic Drugs (HFD-600). A 505(b)(2) applicant shall send the notification to the appropriate division in the Center for Drug Evaluation and Research reviewing the application. A patent owner or its representative may also notify FDA of the filing of any legal action for patent infringement. The notice should contain the information and be sent to the offices or divisions described in this paragraph.

(3) If the patent owner or approved application holder who is an exclusive patent licensee waives its opportunity to file a legal action for patent infringement within 45 days of a

receipt of the notice of certification and the patent owner or approved application holder who is an exclusive patent licensee submits to FDA a valid waiver before the 45 days elapse, approval of the abbreviated new drug application or the 505(b)(2) application will be made effective upon completion of the agency's review and approval of the application. FDA will only accept a waiver in the following form:

> (Name of patent owner or exclusive patent licensee) has received notice from (name of applicant) under (section 505(b)(3) or 505(j)(2)(B) of the act) and does not intend to file an action for patent infringement against (name of applicant) concerning the drug (name of drug) before (date on which 45 days elapses. (Name of patent owner or exclusive patent licensee) waives the opportunity provided by (section 505(c)(3)(C) or 505(j)(B)(iii) of the act) and does not object to FDA's approval of (name of applicant)'s (505(b)(2) or abbreviated new drug application) for (name of drug) with an immediate effective date on or after the date of this letter.

APPENDIX F

PROPOSED RULES
DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
21 CFR Part 314
64 Fed. Reg. 42,873
(42,873-42,875)

[Docket No. 85N-0214]

180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications

---

Friday, August 6, 1999

SUPPLEMENTARY INFORMATION:

I. Background

The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (the Hatch-Waxman Amendments) created section 505(j) of the act (21 U.S.C. 355(j)). Section 505(j) established the ANDA approval process, which allows a generic version of a previously approved innovator drug to be approved without submission of a full new drug application (NDA). An ANDA refers to a previously approved new drug application (the "listed drug") and relies upon the agency's finding of safety and effectiveness for that drug product.

Innovator drug applicants must include in an NDA information about patents for the drug product that is the subject of the NDA. FDA publishes this patent information as part of the agency's publication "Approved Drug Products with Therapeutic Equivalence Evaluations" (the Orange Book).

Generic drug applicants must include in an ANDA a patent certification described in section 505(j)(2)(A)(vii) of the act for each patent listed in the Orange Book for the listed drug. The applicant must certify one of the following for each patent: (1) that no patent information on the drug product that is the subject of the ANDA has been submitted to FDA; (2) that such patent has expired; (3) the date on which such patent expires; or (4) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted. These certifications are known as "paragraph I," "paragraph II," "paragraph III," and "paragraph IV" certifications, respectively.

Notice of a paragraph IV certification must be provided to each owner of the patent (patent owner) that is the subject of the certification and to the holder of the approved NDA (NDA holder) to which the ANDA refers. The terms "patent owner" and "NDA holder" as used throughout this proposed regulation mean either those parties or their representatives, including exclusive licensees. The agency recognizes that different terms are used throughout other sections of the regulations for the idea expressed in section 505(j)(2)(B)(i)(I) and (j)(2)(B)(i)(II) of the act that notice must be given to the principals (patent owner and NDA holder) or their representatives. The agency has added a definitions section to the proposed regulation to clarify the meaning of these terms, as well as other terms, as used in this section.

The submission of an ANDA for a drug product that is claimed in a patent is an infringing act if the ANDA product is intended to be marketed before expiration of the patent. (See 35 U.S.C. 271(e)(2).) Therefore, the submission of an ANDA with a paragraph IV certification may be the basis for patent infringement litigation.

Given this risk of patent infringement litigation, section 505(j)(5)(B)(iv) [1] of the act provides an incentive for generic drug applicants to file paragraph IV certifications challenging patents that may be invalid, unenforceable, or not infringed by the product that is the subject of the ANDA.

Prior to the enactment of the Food and Drug Administration Modernization Act of 1997 (the Modernization Act), 180-day exclusivity was described at section 505(j)(4)(B)(iv) of the act. The Modernization Act added new provisions to section 505(j) that resulted in a renumbering of the sections.

In certain circumstances, the first applicant whose ANDA contains a paragraph IV certification is protected from competition from subsequent generic versions of the same drug product for 180 days from either the date the first applicant's drug product is first commercially marketed or the date of a final court decision holding the patent that is the subject of the paragraph IV certification invalid, unenforceable, or not infringed. This marketing protection is commonly known as "180-day exclusivity."

In the Federal Register of October 3, 1994 (59 FR 50338), FDA published the final rule implementing the patent

---

[1] Section 505(j)(5)(B)(iv) of the act states that:

If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing [sic] such a certification, the application shall be made effective not earlier than one hundred and eighty days after—

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.

and marketing exclusivity provisions of the Hatch-Waxman Amendments. Section 314.107(c)(1) (21 CFR 314.107(c)(1)), the regulation implementing section 505(j)(5)(B)(iv) of the act, provided:

> If an abbreviated new drug application contains a certification that a relevant patent is invalid, unenforceable, or will not be infringed and the application is for a generic copy of the same listed drug for which one or more substantially complete abbreviated new drug applications were previously submitted containing a certification that the same patent was invalid, unenforceable, or would not be infringed and the applicant submitting the first application has successfully defended against a suit for patent infringement brought within 45 days of the patent owner's receipt of notice submitted under § 314.95, approval of the subsequent abbreviated new drug application will be made effective no sooner than 180 days from whichever of the following dates is earlier:
>
> (i) The date the applicant submitting the first application first commences commercial marketing of its drug product; or
>
> (ii) The date of a decision of the court holding the relevant patent invalid, unenforceable, or not infringed.

(Emphasis added)

FDA's requirements for 180-day exclusivity were successfully challenged in the courts in *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998), and *Granutec, Inc. v. Shalala*, No. 97-1873 and No. 97-1874, 1998 U.S. App. LEXIS 6685 (4th Cir. Apr. 3, 1998).

Following the *Mova* circuit court decision, on June 1, 1998, the district court entered an order stating that the successful

defense requirement of § 314.107(c)(1) is invalid and permanently enjoined FDA from enforcing it. In the Federal Register of July 14, 1998 (63 FR 37890), FDA published a guidance for industry entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act" (June 1998), describing its approach to 180-day exclusivity in light of the court decisions. In the Federal Register of November 5, 1998 (63 FR 59710), the agency published an interim rule revoking the "successful defense" requirement. Since that time the agency has regulated directly from the statute when making exclusivity decisions on a case-by-case basis.

The agency is proposing new regulations to address the issues that have arisen as a result of the *Mova* and *Granutec* decisions and to respond to other matters related to 180-day exclusivity not currently addressed by the regulations. Consistent with the legislative purpose of section 505(j)(5)(B)(iv) of the act, the proposed regulations continue to provide an incentive for challenging a listed patent, while at the same time preventing prolonged or indefinite delays in the availability of generic drug products.

During litigation of the many cases related to 180-day exclusivity, the parties and courts have recognized the potential for the 180-day exclusivity process to substantially delay the entry of competitive generic drug products into the market. This situation can occur when the marketing of any subsequent generic drug product is contingent upon the occurrence of an event that is within the first ANDA applicant's control. Such delays could result, for example, from the inability of the first ANDA applicant with a paragraph IV certification to obtain timely approval of its application and begin commercial marketing of its product.

Licensing agreements and other arrangements between an innovator company and the generic drug company who is the first ANDA applicant to file a paragraph IV certification can

be of considerable financial benefit to the companies involved, but also may contribute to delayed generic competition by forestalling the beginning, or triggering, of the 180-day exclusivity period. These arrangements can create almost insurmountable barriers to the final approval and marketing of generic drug products that are otherwise ready for final approval. These barriers thwart a major congressional goal underlying the passage of the Hatch-Waxman Amendments.

In developing the approach described in this proposal, the agency has been guided by the text of the statute, opinions rendered by courts that have addressed these issues, and concerns expressed to the agency in submissions commenting on the June 1998 guidance and November 1998 interim rule. The agency has also been guided by its 15 years of experience with the 180-day exclusivity provisions. This experience has provided FDA with valuable information regarding the influence of the 180-day exclusivity provisions on the ANDA approval process and the marketing of generic drug products.

* * *

NOTICES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

63 Fed. Reg. 37,890

[Docket No. 98D-0481]

Guidance for Industry on 180-Day Generic ~~Drug~~ Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act; Availability

---

Tuesday, July 14, 1998

SUPPLEMENTARY INFORMATION: A requirement of FDA's regulations implementing the 180-day generic drug exclusivity provisions of the act has recently been successfully challenged in court. Section 314.107(c)(1) (21 CFR 314.107(c)(1)) applies and interprets section 505(j)(5)(B)(iv) of the act (21 U.S.C. 355(j)(5)(B)(iv)). Section 314.107(c)(1) contains the "successful defense" provision, which requires an abbreviated new drug application (ANDA) applicant to be sued for patent infringement and to prevail in the litigation in order to receive the 180-day period of marketing exclusivity. Two recent circuit court decisions, *Mova Pharmaceutical Corp. v. Shalala*, No. 97-5082, 1998 U.S. App. Lexis 7391 (D.C. Cir. Apr. 14, 1998) and *Granutec, Inc. v. Shalala*, No. 97- 1873 and No. 97-1874, 1998 U.S. App. LEXIS 6685, (4th Cir. Apr. 3, 1998), held that the "successful defense" requirement was not supported by the act. The effect of these decisions, together with a June 1, 1998, order of the district court in *Mova*, is that FDA will not enforce the "successful defense" provisions of § 314.107(c)(1).

-FDA intends to formally remove the "successful defense" provisions from § 314.107(c)(1), but that process is not complete. Following withdrawal of the regulatory provision, FDA expects to begin a rulemaking to issue new regulations under section 505(j)(5)(B)(iv) of the act. In the meantime, the agency must make exclusivity decisions for ANDA's that are nearing approval. Until such time as the rulemaking process is complete, FDA will regulate directly from the statute and will make decisions on 180-day generic drug exclusivity on a case-by-case basis.

-The guidance is intended to provide industry with information on how FDA is applying section 505(j)(5)(B)(iv) of the act in light of the decisions in *Mova* and *Granutec*. The agency will revise this guidance as additional interpretations are made.

-The guidance is being implemented immediately without prior public comment because the guidance is needed to explain FDA's application of the statute in light of recent court decisions. However, the agency wishes to solicit comment from the public and is providing a 90-day comment period and establishing a docket for the receipt of comments.

-This guidance is a level 1 guidance consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). It represents the agency's current thinking on 180-day generic drug exclusivity under the Hatch-Waxman Amendments. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the act.

-Interested persons may submit written comments on the guidance to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in

the heading of this document. The guidance and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: July 7, 1998.

William B. Schultz,

Deputy Commissioner for Policy.

RULES and REGULATIONS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
21 CFR Part 314
62 Fed. Reg. 63,268

[Docket No. 85N-0214]

Policy on 180-Day Marketing Exclusivity for Drugs Marketed Under Abbreviated New Drug Applications; Clarification

---

Friday, November 28, 1997

SUPPLEMENTARY INFORMATION:

I. Background

The 1984 amendments included a provision, codified under section 505(j)(4)(B)(iv) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(j)(4)(B)(iv)), granting 180 days of marketing exclusivity to the first applicant to submit an ANDA containing a challenge to a listed patent. Regulations interpreting this provision were proposed in 1989 (54 FR 28872, July 10, 1989), and made final in 1994 (59 FR 50338, October 3, 1994). These regulations are codified under § 314.107(c) (21 CFR 314.107(c)).

The regulations state that for a generic drug to qualify for 180 days of marketing exclusivity, the first ANDA applicant submitting a certification under section 505(j)(2)(A)(vii)(IV) of the act (paragraph IV certification) to the listed patent must, in addition to submitting the certification, be sued for patent infringement and successfully defend that suit (§ 314.107(c)). This interpretation has been the subject of legal action in *Inwood Laboratories, Inc. v. Young*, 723 F. Supp. 1523 (D.D.C. 1989), *vacated as moot*, 43 Fed.3d 712

(D.C.Cir. 1989); *Mova Pharmaceutical Corp. v. Shalala*, 955 F. Supp. 128 (D.D.C. 1997), and *Granutec, Inc. et al. v. Shalala et al.*, No. 5:97-CV-485-BO(1)(E.D.N.C. July 3, 1997). Both the *Inwood* and *Mova* courts held that 180 days of marketing exclusivity should be granted to the first ANDA applicant who files a paragraph IV certification, regardless of whether the applicant is subsequently sued for patent infringement. The *Mova* decision has been appealed to the U.S. Court of Appeals for the District of Columbia Circuit.

Following the *Mova* decision, in June 1997, the Office of Generic Drugs notified applicants with ANDA's for ranitidine hydrochloride (HCl) that the agency would acquiesce to the court's holding in *Mova*, pending an appellate decision. The agency determined that temporarily acquiescing to the court's holding in *Mova* would promote administrative uniformity in the application of section 505(j)(4)(B)(iv) of the act and would prevent forum shopping among disappointed ANDA applicants. Subsequently, the U.S. District Court for the Eastern District of North Carolina addressed the validity of § 314.107(c) in *Granutec v. Shalala*, and, in a holding contrary to the earlier Mova decision, ordered FDA to follow its regulations in approving ANDA's for ranitidine HCl. The Granutec decision wasstayed and is on expedited appeal to the U.S. Court of Appeals for the 4th Circuit.

Because the uncertain state of the law makes it difficult for the industry to make business plans and other arrangements, CDER wishes to clarify its policy with respect to these exclusivity issues, pending their final resolution by the courts.

II. 180-Day Marketing Exclusivity

It is the agency's position that, given the uncertainty created by the conflict among the courts, the most reasonable policy is to apply the 180-day exclusivity provisions of the statute as set forth in § 314.107(c) to all ANDA's to which the regulation would, on its face, apply, whether they were

submitted before or after the *Mova* decision. The only ANDA's to which the agency applied the *Mova* analysis, other than those ANDA's directly involved in the *Mova* litigation, were those for ranitidine HCl.

The regulations in § 314.107(c) were issued through notice and comment rulemaking with the active participation of the pharmaceutical industry and consumer groups. They are the product of careful consideration by the agency of the complex factors at issue in granting a period of exclusivity to generic drug applicants and in ensuring that the statute is implemented in a manner most consistent with its original purpose. These regulations will be applied until such time as the appellate courts complete their analyses of the agency's interpretation.

III. Approval of ANDA's After Judgment in the District Courts

The agency does not intend to acquiesce to the court's decision in *Torpharm v. Shalala*, Civil Action No. 97-1925 (JR) (D.D.C. Sept. 15, 1997), in which the court, finding that the term "the court" in section 505(j)(4)(B)(iii) of the act means district court, ordered FDA to approve an ANDA after the applicant had prevailed in patent infringement litigation in the district court, but before either the appeal was resolved or the 30-month stay had lapsed. The U.S. Court of Appeals for the District of Columbia has granted the appeal of *Torpharm* an expedited review. While *Torpharm* is pending on appeal, FDA will continue to interpret the statute as described in § 314.107(e), which defines "the court" as "the court that enters final judgment from which no appeal can be or has been taken."

Dated: November 7, 1997.

Roger Williams,

Deputy Center Director for Pharmaceutical Science.

RULES and REGULATIONS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
21 CFR Part 314
59 Fed. Reg. 50,338
(50,350-50,356)

[Docket No. 85N-0214]

RIN 0905-AB63
Abbreviated New Drug Application Regulations;
Patent and Exclusivity Provisions

Monday, October 3, 1994

---

* * *

I. Section 314.10—Effective Date of Approval of a 505(b)(2) Application or Abbreviated New Drug Application Under Section 505(j) of the Act)

Proposed § 314.107 was intended to codify the requirements under section 505(c)(3) and (j)(4) of the act regarding the effective dates of approval for a 505(b)(2) application or an ANDA. For example, if the 505(b)(2) applicant or ANDA applicant certified that there are no relevant patents, that patent information has not been submitted, that the patent has expired, or that the patent is invalid, unenforceable, or not infringed, and the patent owner has not brought suit for patent infringement, proposed § 314.107(b)(1) would treat the date FDA issues an approval letter as the effective date of approval. If the 505(b)(2) applicant or ANDA applicant certified that the patent would expire on a specific date, proposed § 314.107(b)(2) would treat that specific date as the effective date of approval. Proposed § 314.107(b)(3) described several situations in which the effective date of approval could vary, depending upon the disposition of patent litigation.

Proposed § 314.107 also implemented the "180-day exclusivity period" described in section 505(j)(4)(B)(iv) of the act. In brief, section 505(j)(4)(B)(iv) of the act states that if an ANDA contains a paragraph IV patent certification (declaring the patent to be invalid or not infringed) and the ANDA is for a drug for which a previous ANDA containing a paragraph IV patent certification has been submitted, approval of the subsequently submitted ANDA will be made effective 180 days after the date FDA receives from the previous ANDA applicant notice of the first commercial marketing of the drug or the date a court holds the patent that is the subject of the patent certification to be invalid or not infringed, whichever date is earlier (see section 505(j)(4)(B)(iv) of the act). Proposed § 314.107(c) provided that an applicant must be the first ANDA applicant to submit a substantially complete application with a paragraph IV certification and must have been sued for patent infringement in order to qualify for 180-day exclusivity.

64. One comment asked FDA to permit any person to contact FDA informally to determine whether the listed patent information was correct and later petition the agency to correct any errors. As proposed, § 314.107 did not provide for inquiries concerning patent information.

Sections 314.53(f) and 314.94(a)(12)(vii) describe the procedures that an applicant can use to question the validity of patent information. In brief, if an applicant disputes the accuracy or relevance of patent information, it should first notify FDA in writing and state the reasons for the disagreement. FDA will then request that the relevant NDA holder confirm the validity of the patent information, but will not change the patent information itself unless the NDA holder withdraws or amends the patent information. The agency believes that these procedures for determining the validity of patent information are sufficient, and, therefore, declines to adopt the change suggested by the comment.

65. FDA, on its own initiative, has amended § 314.107(b)(1) to state that an approval will become effective on the date FDA issues an approval letter except as provided under paragraphs (b)(3), pertaining to approvals resulting from the disposition of patent litigation; (b)(4), pertaining to approvals where an applicant has submitted multiple certifications; and (c), regarding subsequent ANDA submissions. These changes are to clarify that there are other situations that may make an approval effective.

66. Two comments would revise proposed § 314.107(b)(1)(iv) regarding a certification that a patent is "invalid or will not be infringed." The comments would have this certification state that the patent is "invalid and will not be infringed."

FDA declines to adopt the suggested language. The provision simply paraphrases the statutory language for a paragraph IV certification (see section 505(j)(2)(A)(vii)(IV) of the act). The agency has, however, amended the provision to account for a certification that a patent is unenforceable and, as stated earlier, removed the language regarding consent from the patent holder.

67. One comment asked FDA to amend proposed § 314.107(b)(1)(iv)(B)(2) to require NDA holders to have a role in or consent to licensing agreements between patent owners and ANDA applicants. The proposed rule would consider the effective date of approval for a 505(b)(2) application or an ANDA to be the date FDA issues an approval letter if, among other things, the drug product is covered by a patent licensing agreement and the 505(b)(2) application or ANDA contains a statement that the applicant has been granted a patent license and a statement from the patent owner that it has a licensing agreement with the applicant for the proposed drug product and that the patent owner consents to an immediate effective date.

As stated elsewhere in this final rule, FDA believes that the negotiations surrounding licensing agreements and the parties entering into such agreements are outside the scope of this rule. Additionally, as stated in the response to comment 43 above, the agency has deleted the provisions in § 314.107(b)(1)(iv) relating to consent by a patent owner to an immediate effective date of approval for a licensee.

68. The agency, on its own initiative, has made minor grammatical changes and other revisions to § 314.107 (b)(2) and (b)(3). These revisions replace "Upon patent expiration" with "Patent Expiration" and "Upon disposition of patent litigation" with "Disposition of patent litigation." Additionally, the changes specify that the patent owner must receive the notice of certification and clarify, in § 314.107(b)(3)(i)(B), the effective date of approval.

69. Proposed § 314.107(b)(3) described the effective date of approval of a 505(b)(2) application or ANDA upon disposition of patent litigation. Under proposed § 314.107(b)(3)(i)(A), if an applicant certified that the relevant patent was invalid or would not be infringed, and the patent owner or its representative brought suit for patent infringement, the effective date of approval for the 505(b)(2) application or ANDA would be 30 months after the date of receipt of the notice of certification of patent invalidity or noninfringement by the patent owner or its representative unless a court extended or reduced the 30-month period. Proposed § 314.107(b)(3)(i)(B) described the effective date of approval of a 505(b)(2) application or an ANDA upon disposition of patent litigation when the patented drug product also qualified for 5 years of market exclusivity. Proposed § 314.107(b)(3)(ii) through (b)(3)(iv) represented additional modifications to the effective date of approval due to court decisions or orders.

One comment concerned the proposed language in § 314.107(b)(3)(i) regarding the 30-month period. The

comment would amend this provision to shorten or lengthen the 30-month period pursuant to a court order.

The suggested change is unnecessary because § 314.107(b)(3)(i) through (b)(3)(iv) explains how the 30-month period may be changed due to court decisions or orders.

The agency also emphasizes that disposition of patent litigation will not result in automatic approval of a pending application. FDA notes that section 505(c)(3)(C) and (j)(4)(B)(iii) of the act describe when approval of a 505(b)(2) application or an ANDA shall be made effective if an applicant submitting a 505(b)(2) application or ANDA has made a paragraph IV certification and has or has not been sued for patent infringement. For example, if the applicant made a paragraph IV certification, was sued for patent infringement, and the court hearing the patent infringement suit decided that the patent was either invalid or not infringed, section 505(c)(3)(C)(i) and (j)(4)(B)(iii)(I) of the act state, respectively, that approval of the 505(b)(2) application or ANDA may "be made effective on the date of the court decision." However, the agency interprets these provisions of the act as requiring, as a preliminary matter, final agency approval of the application in order for any approval to be made effective. Thus, an applicant with a tentative approval may not begin marketing its drug product until it has received an approval letter from the agency because a tentative approval letter does not constitute a final "approval" of the application. In such cases, the agency will examine the application to determine whether there have been any changes in the conditions under which the application was tentatively approved. The tentative approval would become final and, therefore, effective only when the agency sends an approval letter to the applicant.

Similarly, an applicant that has not yet received a tentative approval letter may not begin marketing its drug product in

the event that a court reaches a decision in any related patent infringement litigation because there is no final "approval" by FDA that could be made "effective" within section 505(c)(3)(C)(i) or (j)(4)(B)(iii) of the act.

Other provisions of the act support this interpretation of section 505(c)(3)(C)(i) and 505(j)(4)(B)(iii) of the act as they relate to the expiration of the 30-month period or the date of the court decision. For example, section 505(j)(3) of the act states that the agency shall approve an ANDA unless certain circumstances are found to exist. Section 505(j)(3)((A) of the act prevents the agency from approving an ANDA if the agency finds that "the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity." Consequently, until FDA assesses the available information, often from an additional current good manufacturing practices inspection, it cannot determine whether the applicant's methods and controls used for the manufacture, processing, and packing of the drug are adequate to assure and preserve the drug's identity, strength, quality, and purity and therefore, under section 505(j)(3) of the act, whether the ANDA should be approved. Thus, unless FDA has formally approved an ANDA under section 505(j)(3) of the act, there is no "approval" that could be made effective under section 505(j)(4)(B) of the act upon resolution of the patent litigation. (Section 505(d) of the act establishes an analogous approval requirement for 505(b)(2) applications.)

The legislative history provides additional support for FDA's interpretation. In describing the provisions regarding effective dates of approval and court decisions, the House Report states:

> The Committee wishes to emphasize that the court may not order an ANDA approved under this provision.

> These are times when approval of an ANDA may be made effective if the FDA has approved the ANDA.

See H. Rept. 857, 98th Cong., 2d sess., Part 1, 27-28 (1984) (emphasis added). The same concept is applicable to 505(b)(2) applications (*see id.* at 34).

This interpretation of section 505(j)(4)(B) of the act reflects current FDA practice and revises the agency's previous policy that was stated in the preamble to the proposed rule (see 54 FR 28872 at 28894). It also clarifies the agency's position on delayed effective dates of approvals as expressed in the preamble to the final rule on ANDA content and format that was published in the Federal Register on April 28, 1992 (57 FR 17950 at 17956). Consequently, FDA, on its own initiative, has amended § 314.107(b)(3) to clarify when approval of an application may become effective and by adding a new paragraph (b)(3)(v) to state that, in order for an approval to become effective under paragraph (b)(3), the applicant must first receive a final approval letter from the agency.

70. One comment would restrict proposed § 314.107(b)(3)(ii) to district court orders. The comment would revise the rule to state: "If before the expiration of the 30-month period, or 7 1/2 years where applicable, the district court decides such patent is invalid or not infringed, the approval will be made effective on the date of the district court order or judgment." The comment would also replace the words "a final order" in proposed § 314.107(b)(3)(iii) and (b)(3)(iv) with "an order or judgment."

FDA declines to limit the rule to district court orders. As stated in the preamble to the proposed rule, FDA interprets the requirement of a "court decision" to mean "a final decision of a court from which no appeal can or has been taken" (*see* 54 FR 28872 at 28895). Beginning the 180-day exclusivity period before the resolution of the appeals process

would render the exclusivity valueless to a prudent applicant who delayed marketing until the issues were resolved on appeal.

FDA has, however, revised § 314.107(b)(3)(iii) and (b)(3)(iv) to refer to an "order or judgment" because both terms are sometimes used to refer to actions that terminate an action or decide a matter in litigation.

71. Proposed § 314.107(b)(4) concerned applicants who made multiple patent certifications. In essence, the proposed provision would consider the approval of a 505(b)(2) application or an ANDA to be effective on the last applicable date. One comment would amend proposed § 314.107(b)(4) by adding a new sentence stating:

> If the applicant has submitted certifications under § 314.50(i) or § 314.94(a)(12) and has submitted notice to the owner of the patent pursuant to § 314.95, and FDA subsequently receives a stipulation or order by the district court notifying it that the applicant has amended its answer to add new arguments, not included in that notice, in any ensuing suit for patent infringement, the date of approval will be calculated based on a 30-month period starting at the date of receipt by FDA of each such stipulation or order, and the approval will become effective on the last applicable date.

Alternatively, the comment suggested that an ANDA applicant who amended its answer to a patent infringement suit to include arguments that were not in the notice to the patent owner under § 314.95 would be considered to have been uncooperative in expediting the lawsuit. The comment explained that these revisions would prevent generic drug companies from amending their answers during patent infringement litigation to delay completion of a trial and also delay the start of the 30-month period.

FDA declines to adopt the comment's suggestion. As stated above, FDA has revised the notice requirements in § § 314.52(c) and 314.95(c) to parallel the statutory language rather than specify notice requirements. The agency has neither the resources nor the expertise to engage in patent disputes or questions regarding sufficiency of notice. The statute leaves the issue of extending the 30-month period (based on a lack of cooperation between the parties in patent litigation) to the discretion of the trial court. The agency believes that the trial court should make determinations of cooperation on a case-by-case basis. Accordingly, the agency declines to amend the rule to consider an applicant to be uncooperative and to extend the 30-month period if the applicant amends an answer to a complaint in patent litigation to include an argument not reflected in the notice to the patent holder.

72. FDA received several comments on proposed § 314.107(c) and the 180-day exclusivity period against subsequent ANDA's. As proposed, § 314.107(c) would provide 180-day exclusivity to the first ANDA applicant that made a paragraph IV patent certification (that the patent was invalid or not infringed) and was sued for patent infringement. Seven comments said the language requiring an ANDA applicant to have been sued in order for the 180-day exclusivity period to become effective was contrary to the statute and to a judicial ruling in the U.S. District Court for the District of Columbia.

Section 505(j)(4)(B)(iv) of the act can be applied straightforwardly only when an applicant who seeks the 180-day period of exclusive marketing has been involved in a patent infringement lawsuit. To apply the section where there has been no lawsuit would require that the agency ignore the textual relationship between section 505(j)(4)(B)(iii) and (j)(4)(B)(iv) of the act and assume that Congress intended, contrary to the goals it stated in the legislative history, to

create an incentive for delay in generic competition, without any countervailing benefit to society. Moreover, it would provide a windfall to an applicant who has not devoted the considerable time and money necessary for patent litigation. Thus, consistent with the agency's longstanding interpretation of the act, § 314.107(c) applies only when the first applicant has been sued. Although, as the comments state, one Federal district court reached a contrary conclusion, the agency appealed that decision and, on appeal, the decision was vacated as moot (*Inwood Laboratories, Inc. v. Young*, 723 F.Supp. 1523 (D.D.C. 1989), vacated as moot, no. 89-5209 (D.C. Cir., November 13, 1989). The agency has not altered its interpretation of the act.

FDA has, however, revised § 314.107(c) to clarify other issues, such as the start and end of the 180-day exclusivity period, and to make minor editorial changes.

73. One comment suggested revising proposed § 314.107(c) to state that the 180-day exclusivity period does not apply to delay the effective date of approval of licensees to the NDA holder.

As stated above, FDA does not believe that an ANDA applicant who has made a paragraph IV certification and obtained a patent license should be able to circumvent a 180-day exclusivity period. Consequently, the agency declines to amend the provision as requested by the comment.

74. Two comments would revise proposed § 314.107(c) to extend the 45-day period in which patent owners have to file suit against an ANDA applicant. The proposal referred to the statutory 45-day period in which a patent owner would have to file suit against an ANDA applicant. The comments would extend the 45-day period upon request or when the ANDA applicant and the patent owner agree to an extension.

FDA declines to accept the comments' suggestion. The 45-day period for filing a lawsuit against an ANDA applicant

is fully consistent with section 505(j)(4)(B)(iii) of the act, and the agency finds that there are sound policy reasons that outweigh extensions of the 45-day period. For example, if an ANDA applicant has provided notice to a patent owner stating that the ANDA applicant believes that the patent is invalid or would not be infringed (a paragraph IV certification), the patent owner may elect to bring suit against the ANDA applicant for patent infringement. If the suit is brought within 45 days from the date the ANDA applicant provided the notice, section 505(j)(4)(B)(iii) of the act precludes the agency from granting a final approval of the ANDA. If suit is not brought within 45 days, FDA could grant a final approval of the ANDA upon expiration of this time period, assuming that the ANDA met all applicable requirements for approval. Thus, amending the rule to provide the patent owner an extension to file suit beyond the 45-day period would not prevent the agency from approving ANDA's during the extension (because the statutory restriction against making an approval effective would no longer apply), even if the patent owner later decided to bring suit against the ANDA applicant and prevailed in that lawsuit. Such a result would waste agency and industry resources.

FDA also notes that, in situations where an ANDA applicant has amended its notification to the patent owner and approved NDA holder to make it more complete, the agency may, under § 314.95(f), consider the 45-day period to begin on the day after the date of receipt of the amended notification.

75. One comment would revise proposed § 314.107(c) to begin the 180-day exclusivity period "on the first day that a court would allow non-infringing marketing (unless that decision were stayed)" or "30 months from receipt of notice."

The agency declines to revise the rule as suggested. The rule, which paraphrases the statutory language at section 505(j)(4)(B)(iv) of the act, better reflects the plain meaning of

the act. Revising the rule as requested by the comment would begin the 180-day exclusivity period at the end of the 30-month period without regard to whether the applicant had commenced marketing on that date.

76. Proposed § 314.107(c)(1)(i) would provide 180-day exclusivity to the first ANDA applicant to submit a complete ANDA with a paragraph IV patent certification and "to be sued within 45 days of the patent owner's receipt of notice." One comment said the rule, as drafted, created an incentive for frivolous claims of patent invalidity or noninfringement because it would give ANDA applicants exclusivity even if the applicant was unsuccessful in defending against the patent owner's lawsuit. The comment would replace the phrase "to be sued within 45 days" with "and to successfully defend a suit brought within 45 days."

FDA agrees and has amended § 314.107(c) accordingly.

77. FDA received several comments regarding proposed § 314.107(c)(1)(i) and (c)(1)(ii). These provisions concerned the start of the 180-day exclusivity period. Proposed § 314.107(c)(1)(i) would begin the 180-day exclusivity period on the date of the first commercial marketing of the drug product by the first ANDA applicant who submitted a substantially complete ANDA containing a certification that the patent was invalid or not infringed and who was sued for patent infringement within 45 days after providing notice to the patent owner. Alternatively, proposed § 314.107(c)(1)(ii) would begin the 180-day exclusivity period on the "date a decision of the court holding the relevant patent invalid or not infringed" if that date was earlier than the date of the first commercial marketing. One comment would revise proposed § 314.107(c)(1)(ii) to include a cross-reference to the language in § 314.107(b)(3) on patent litigation.

FDA declines to adopt the suggested revision. The agency believes that the meaning of § 314.107(c)(1)(ii) is sufficiently

clear so that the court referred to in § 314.107(c)(1)(ii) is the court deciding the patent infringement suit. However, for reasons stated elsewhere in this document, the agency has amended this provision to include a reference to unenforceable patents.

78. One comment would amend § 314.107(c), (c)(1)(i), and (c)(1)(ii) to permit an ANDA applicant to decide whether to start the 180-day exclusivity period on the date it notifies the agency that the applicant has begun commercial marketing of the drug product or to wait to see whether the court decision is appealed. If an appeal did result, the comment would permit the ANDA applicant to have the 180-day period begin when a court issues a decision on the appeal.

FDA declines to amend the provision as suggested by the comment. The provision is consistent with section 505(j)(4)(B)(iv) of the act by beginning the 180-day period on the date the first ANDA applicant has notified the agency that it has begun commercial marketing of the drug product or the date of a court decision holding the patent to be invalid or not infringed, "whichever is earlier" (see section 505(j)(4)(B)(iv) of the act).) Allowing an applicant to begin marketing before the commencement of the 180-day exclusivity period would, in effect, extend the exclusivity period in a manner that is inconsistent with the plain meaning of the act. FDA also notes that the court decision must be a final decision from which no appeal can be or has been taken (*see* 54 FR 28872 at 28895).

79. FDA received four comments regarding "substantially complete" applications under proposed § 314.107(c)(2). Proposed § 314.107(c)(2) would consider an ANDA to have been "previously submitted" with respect to another application for the same listed drug "if the date on which the first application was both substantially complete and contained a certification that the patent was invalid or not infringed is earlier than the date on which the second

application was both substantially complete and contained the same certification." The proposal also stated that a "substantially complete" application "must contain the results of any required bioequivalence studies, or, if applicable, a request for a waiver of such studies."

One comment asked FDA to provide information as to which ANDA was the first "substantially complete" ANDA. The comment suggested that disclosing such information did not present any confidentiality problems because the ANDA applicant would have revealed the existence of the ANDA when it provided notice of certification of invalidity or noninfringement of the patent to the patent owner and NDA holder.

FDA agrees, in part, with the comment. Disclosing whether an ANDA had been received for a specific listed drug would enable manufacturers to decide whether to develop a generic version of that drug and perhaps conserve the manufacturer's resources. Such knowledge could, in turn, effectively reduce the number of applications for the same product and thus also conserve agency resources. The agency, therefore, will disclose whether an ANDA has been received for a particular drug, but, in order to preserve the confidentiality of the applicant, will not disclose when the application had been received or the applicant's identity. Potential applicants who wish to inquire whether an ANDA for a specific drug has been received can contact the Regulatory Support Branch (HFD-615), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-594-0315.

80. Two comments disagreed with the language regarding "substantially complete" applications. One comment said FDA should only determine whether an ANDA contains a bioequivalence test or waiver request and not focus on the results of any required bioequivalence studies. The second comment suggested that a "substantially complete" ANDA be

one that contained a paragraph IV patent certification and a bioequivalence study that is ultimately approved. The comment said this change would deter ANDA applicants from submitting "superficial" bioequivalence tests. The comment also suggested that the agency establish criteria as to whether changes to an ANDA were so substantial that the ANDA could no longer be considered as the first to be filed.

Since publication of the proposed rule, FDA has clarified its policies regarding the submission of incomplete ANDA's. Under the earlier policy, ANDA applicants could submit ANDA's with bioequivalence study protocols and could provide bioequivalence study data at a later date. This policy resulted in a significant and unwarranted expenditure of resources in reviewing applications that had little potential for approval. Thus, in the Federal Register of April 28, 1992, FDA announced that it would no longer accept an ANDA that does not contain complete bioequivalence study data if such data are required for approval (*see* 57 FR 17950 at 17959). A "substantially complete" application, therefore, should have a complete bioequivalence study, or other information to show bioequivalence that could support approval of the application. FDA will examine the bioequivalence information upon submission and, if the agency determines that the bioequivalence information is facially insufficient to support a finding of bioequivalence, the agency will not review the application under § 314.101(d). A decision by the agency after receipt of an application that the bioequivalence information is inadequate for approval does not necessarily mean that the application was not substantially complete at the time of submission.

FDA also declines to establish criteria to establish whether changes to an ANDA were so substantial that it could not be considered to have been filed. While certain changes in an ANDA (e.g., a change in the listed drug) would amount to a new filing for purposes of § 314.107(c)(2), other changes

(e.g., minor labeling changes) would not. The agency believes a case-by-case approach is preferable because many products and manufacturers may be unique.

81. The agency, on its own initiative, has revised the provisions in § 314.107 (c)(2) and (c)(3) to clarify their intent. These provisions address the issues of the "applicant submitting the first application" for exclusivity purposes, what constitutes a "substantially complete" application, and the effective dates of approval for subsequently submitted applications if the first applicant is not "actively pursuing" approval. FDA has made similar editorial changes at § 314.107(c)(4).

82. Four comments addressed proposed § 314.107(c)(3). The proposed provision would make an ANDA that had been received after FDA had already received an ANDA for the same drug immediately effective if the agency concluded that the first ANDA applicant "is not actively pursuing approval of its abbreviated application." Three comments asked FDA to define the phrase "actively pursuing approval."

For purposes of this rule, the phrase "actively pursuing approval" is intended to encompass a drug sponsor's good faith effort to pursue marketing approval in a timely manner. In determining whether a sponsor is actively pursuing marketing approval, FDA will consider all relevant factors, such as the sponsor's compliance with regulations and the timeliness of its responses to FDA's questions or application deficiencies during the review period.

83. One comment would revise proposed § 314.107(c)(3) to make a subsequently received ANDA immediately effective upon a finding that the first applicant is not actively pursuing approval "if [the subsequent application is] otherwise eligible for an immediately effective approval."

The agency agrees and has amended the provision accordingly. This change will remind applicants that FDA

will make approval of a subsequent abbreviated application immediately effective if it satisfies all applicable requirements and FDA has concluded that the first applicant is not actively pursuing approval of its abbreviated application.

84. FDA received five comments regarding the interpretation of "the court" and court judgments in proposed § 314.107(e)(1). Proposed § 314.107(e)(1) stated that "the court" in § 314.107(b) and (c) referred to "the court that enters final judgment from which no appeal can be or has been taken." Three comments supported the proposal, but two comments argued that FDA had misconstrued the 1984 amendments. One comment argued that the court finding a patent to be invalid or not infringed should be "the court of first instance" or district court because a decision that a patent was invalid or not infringed or a decision to issue an injunction would be done by a district court. Another comment argued that interpreting "the court" to mean the court that enters final judgment "effectively gives a patent owner an additional extension of the patent * * * for the duration of the appeal" and delay generic competition. The comment would revise the rule to permit an ANDA applicant to market its drug product after it had prevailed at the trial court level.

FDA declines to amend § 314.107(e)(1) as suggested by the comments. To construe "the court" as a district court, regardless of any appeal of the district court decision, would deny the benefits of exclusivity to a prudent applicant that delayed marketing its product until resolution of an appeal by the patent holder (*see* 54 FR 28872 at 28894). Moreover, if the patent holder appealed the district court decision and were able to obtain a stay or an injunction against the marketing of the applicant's product, the applicant could lose the entire 180-day exclusivity period before the stay or injunction were lifted.

Given these considerations, FDA believes that any reference to "the court" must be the court that enters final judgment from which no appeal can be or has been taken. (The reference to "appeals" does not include the certiorari process. The likelihood of an appellate court decision being heard and overruled by the Supreme Court is too remote to warrant delaying marketing and exclusivity pending resolution of a petition for writ of certiorari.) This interpretation avoids potentially premature decisions on the effective date of ANDA approval and the loss of 180-day exclusivity. FDA has, however, also revised § 314.107(e)(2) to clarify which court decisions will represent the "final" judgment.

85. One comment would revise proposed § 314.107(e)(2) to refer to a court order or judgment rather than simply a court judgment.

As amended, § 314.107(e)(2) refers to a court "decision," which could be in the form of either an order or a judgment. The agency has also made minor changes to § 314.107(e)(2) to clarify that the court decisions involve patent issues and that a higher court can hold or affirm a lower court decision that a patent is invalid, unenforceable, or not infringed.

86. A second comment would revise proposed § 314.107(e)(2) to require applicants to submit copies of a court order or judgment to the Division of Generic Drugs or "New Drug Evaluation Division (where applicable)."

FDA agrees with the comment, and has added § 314.107(e)(2)(iv) to require applicants to send a copy of a final decision to the Office of Generic Drugs, or to the appropriate division in the Office of Drug Evaluation I or the Office of Drug Evaluation II, whichever is applicable.

87. Proposed § 314.107(f) described how the 45-day period for filing a patent infringement suit would be determined. In brief, under proposed § 314.107(f)(1), the 45-

day period would begin on the day after the date the patent owner or approved application holder, if an exclusive patent licensee, received a notice of certification of invalidity or noninfringement of the patent. Proposed § 314.107(f)(2) would require the 505(b)(2) applicant or ANDA applicant to notify FDA whether an action for patent infringement had been filed. Several comments objected to language in proposed § 314.107(f) that would consider notice to or actions by exclusive licensees to be equivalent to notice to or actions by a patent owner. The comments said that exclusive licensees do not always share the patent owner's interests.

FDA agrees and has revised the rule to remove language that would consider exclusive licensees to be equivalent to patent owners.

88. One comment objected to proposed § 314.107(f)(1) because it would start the 45-day period on the day after the date the patent owner or the approved application holder, if an exclusive patent licensee, received notice of invalidity or noninfringement of a patent. The comment argued that the 45-day period should begin on the day after the date that the patent owner and the approved application holder received notice and, if these dates differed, the latest date should mark the start of the 45-day period.

The agency agrees with the comment and has revised § 314.107(f)(1) to begin the 45-day period on the day after the date the patent owner and the approved application holder have received the applicant's notice of certification of invalidity or noninfringement of a patent.

89. FDA received several comments on proposed § 314.107(f)(2). Absent a notice of an action for patent infringement, the proposal would make the approval of an ANDA or 505(b)(2) application effective immediately upon the expiration of the 45-day period for filing a patent infringement suit or upon FDA's completion of the review

and approval process, whichever is later. The comments noted that the regulation would have ANDA or 505(b)(2) applicants notify FDA whether a patent infringement suit had been filed and asked FDA to permit, by regulation, patent owners to notify FDA whether it had brought suit. Alternatively, some comments would require the ANDA or 505(b)(2) applicant certify that it had not been sued. The comments explained that these changes were necessary because ANDA and 505(b)(2) applicants would have no interest in notifying FDA whether suit had been filed because, without such notice, they could immediately secure effective approval of an application.

The agency has amended § 314.107(f)(2) to permit patent owners or their representatives to notify FDA whether a patent infringement suit has been filed. The statute does not require applicants to certify that they have not been sued, and the agency does not believe such a burden to be necessary.

The agency has also made minor revisions to § 314.107(f)(2) to place more emphasis on an applicant's obligation to notify FDA immediately of the filing of any legal action within 45 days of receipt of a notice of certification.

Additionally, the agency has made a grammatical change in § 314.107(f)(2) to clarify that applicants must send the notification to the Office of Generic Drugs or to the appropriate division in the Center for Drug Evaluation and Research reviewing the application.

90. One comment addressed the requirement in proposed § 314.107(f)(2) that a 505(b)(2) applicant or ANDA applicant notify FDA whether an action for patent infringement had been filed "before the expiration of the 45-day time period or the completion of the agency's review of the application, whichever occurs later." The comment argued that a patent owner had 45 days to file a lawsuit after receiving a notice of

certification of invalidity or noninfringement of a patent and, therefore, a party should have an additional time period beyond the 45-day period for filing an action for patent infringement for notifying the agency whether an action had been filed. The comment would revise the rule to give a party an additional 15 days beyond the 45-day period to notify FDA whether an action for patent infringement had been filed.

The agency declines to revise the rule as suggested. FDA believes it is important to learn immediately if an action for patent infringement is filed before the completion of the 45-day period to avoid an erroneous approval with an immediate effective date.

FDA has, therefore, amended § 314.107(f)(2) to require applicants to notify FDA immediately whether any legal action has been filed. The agency has also amended this subsection to clarify the identity of the "applicant."

91. FDA has, on its own initiative, clarified its notification requirements in § 314.107(f)(2)(iii). As proposed, § 314.107(f)(2)(iii) would have required parties to identify a drug by its established name, but would not have expressly required any identification of the drug if no established name existed. The agency has amended this provision to require identification of the drug product by its established name or, if no established name exists, its active ingredient(s).

92. One comment asked FDA to publish information regarding the status and progress of patent infringement suits so other ANDA applicants could decide whether to intervene in the suit "and ask that the 30-month period be shortened or lengthened in the event that it feels that one or both of the litigants are not reasonably cooperating in expediting the action." Alternatively, the comment asked FDA to permit any interested party to petition the agency "to remove an ANDA from exclusivity considerations if it has not proceeded with

due diligence--either in prosecution of its ANDA or defense of an infringement suit."

FDA believes that ANDA applicants are capable of monitoring the progress of patent litigation without imposing the additional burden of acquiring and publishing information on patent litigation on FDA. The agency, therefore, declines to adopt the comment.

FDA also declines to amend the rule to permit third parties to petition the agency to deny exclusivity to an ANDA due to the ANDA applicant's actions during litigation. Under the statute, the reduction or enlargement of the 30-month period is left to the trial court's discretion. Intervention by the agency is unwarranted.

93. One comment suggested replacing the words, "action to defend," in proposed § 314.107(f)(2)(iv) with the words, "action for patent infringement." The comment said that "action to defend" was not a term of art.

FDA agrees and has adopted the comment.

94. FDA, on its own initiative, has modified the language regarding waivers in § 314.107(f)(3). The change is intended to clarify that the patent owner does not object to FDA's approval of an ANDA or 505(b)(2) application with an immediate effective date and to account for those situations where the ANDA applicant or 505(b)(2) applicant and the patent owner have agreed to extend the 45-day period.

* * *

PROPOSED RULES

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
21 CFR Parts 10, 310, 314, and 320
54 Fed. Reg. 28,872
(28,893-28,896)

[Docket No. 85N-0214]

RIN 0905-AB63
Abbreviated New Drug Application Regulations

Monday, July 10, 1989

---

* * *

K. Delay in the Effective Date of Approval of an ANDA and 505(b)(2) Application Because of the Existence of a Patent

The 1984 Amendments require an important change from previous practice for ANDA's and those 505(b)(2) applications previously handled as paper NDA's with respect to the effective date of their approval. The effective dates of approval of ANDA's and 505(b)(2) applications are dependent on the existence of any patents on the pioneer drug for which the generic applicant is seeking approval (sections 505(j)(4)(B) and 505(c)(3) of the act) and on any periods of exclusive marketing accorded the reference listed drug or other listed drug under the so-called "exclusivity" provisions of the act (sections 505(j)(4)(D) and 505(c)(3)(D) of the act). Thus, an ANDA or 505(b)(2) application may be approved with a delayed effective date, as specified by the agency in its approval letter. No new drug product may be introduced or delivered for introduction into interstate commerce under a full or abbreviated new drug application unless the approval of the application is effective (section 505(a) of the act). The

agency proposes to add new § 314.107 to the regulations to codify the statutory requirements with respect to effective dates of approval of ANDA's and 505(b)(2) applications.

With respect to patent status, proposed § 314.107 provides that approval of an ANDA or 505(b)(2) application, if approval is otherwise warranted, would be made effective in accordance with the following conditions. First, if the applicant certified that there are no relevant patents, or the holder of the approved application for a drug product covered by a relevant patent did not submit to FDA any patent information, or that the relevant patents submitted to FDA have expired, approval of the ANDA or 505(b)(2) application would be made effective immediately.

Second, if the applicant certified that any relevant patents would expire on a certain future date, based on information submitted to FDA, approval of the ANDA or 505(b)(2) application would become effective on that date, unless that date had already passed, in which case the approval would be immediately effective.

Third, if the applicant certified that any relevant patent was invalid or would not be infringed, approval of the ANDA or 505(b)(2) application could be made effective 45 days from the date of the receipt of the notice of certification by the patent owner or the approved application holder who is an exclusive patent licensee, unless the patent owner or exclusive patent licensee filed an action for patent infringement before the 45 days have elapsed. As discussed in part V. section D.1.j. above, FDA proposes to require that an applicant who has obtained a patent license to manufacture a generic copy of a patented drug certify under section 505(b)(2)(A)(iv) or 505(j)(2)(A)(vii)(IV) of the act that the relevant patent is invalid or will not be infringed. Although the statute does not expressly address the effect of patent licensing agreements on effective dates, FDA does not believe that Congress intended to interfere with such

agreements between pioneer and generic drug manufacturers. See section 505(b)(1) of the act (defining applicable patents as those "to which a claim of patent infringement would reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug"). Accordingly, FDA proposes to make the approval of an ANDA or 505(b)(2) application effective immediately where the applicant submits (1) information establishing that the proposed drug is covered by a patent licensing agreement with the patent owner, and (2) a written statement from the patent owner consenting to an immediate effective date. FDA invites comment on this approach.

Even in the absence of a licensing agreement, the patent owner or exclusive patent licensee may waive its opportunity to file an action for patent infringement provided it submits a valid waiver to FDA before the 45 days elapses. Under proposed § 314.107(f)(3), if a patent owner or exclusive patent licensee does not intend to file action for patent infringement against the generic applicant within the 45-day time period and the applicant seeks an effective approval date before the 45-day period has elapsed, the patent owner or exclusive patent licensee must submit to FDA a waiver in the form prescribed in the proposed regulation.

1. The 45-day clock. Both the PMA and the Generic Pharmaceutical Industry Association (GPIA) offered FDA suggested regulatory language designed to ensure that the recipient of a notice of patent certification has the full 45 days in which to decide whether to bring a patent infringement suit. (PMA and GPIA comments filed under Docket No. 85N-0214.) FDA believes its proposed requirements under § 314.52 for an application submitted under section 505(b)(2) of the act and § 314.95 for an ANDA under section 505(j) of the act with respect to documentation of receipt of notice of certification and the proposed requirements in § 314.107 address the concerns of the PMA and GPIA. Under this

proposal, the 45-day clock would begin on the day after the date of receipt by the patent owner or its representative or by the approved application holder if the holder is an exclusive patent licensee of the applicant's notice of certification. Thus, the applicant's return receipt or a letter acknowledging receipt from the patent owner or exclusive patent licensee would be deemed to be legal notice of receipt of the applicant's notification by the patent owner or its representative or exclusive patent licensee. Action would then have to be filed in federal court by the patent owner or exclusive patent licensee before the end of the 45th day.

In computing the 45 days, Saturdays, Sundays, and Federal holidays are included. When, however, the 45th day falls on Saturday, Sunday, or on a Federal holiday, the 45th day would be the next succeeding day that is not a Saturday, Sunday, or a Federal holiday. FDA intends to strictly apply the 45-day statutory time period. Therefore, unless FDA is notified in writing by the ANDA or 505(b)(2) applicant before the expiration of the 45-day time period or before the completion of the review period, whichever is later, of the commencement of legal action for patent infringement within the 45-day time period, approval of the ANDA or 505(b)(2) application may be made effective immediately upon expiration of the 45 days or upon completion of the review process, whichever is later. Even if the commencement of legal action occurs before the ANDA is ready for approval but after the 45-day period has elapsed, the agency will approve the ANDA with an immediate effective date when the application review is complete and satisfactory. Notification by the generic applicant of the filing of a complaint alleging patent infringement shall include: (1) the ANDA or 505(b)(2) application number, (2) the ANDA or 505(b)(2) applicant's name, (3) established name of the drug, if any, strength, and dosage form, and (4) a certification that action to defend the patent, identified by number, has been filed in an appropriate court and the date of the filing. An

ANDA applicant shall submit the notification to FDA's Division of Generic Drugs (HFD-230); a 505(b)(2) applicant shall submit the notification to the appropriate division in the Center for Drug Evaluation and Research reviewing the application.

If an action for patent infringement is filed before the expiration of the 45 days, FDA is precluded from making the approval of the ANDA or 505(b)(2) application effective for a period of 30 months while the matter is in litigation or until a date of a final decision determined by a court, with one exception. The exception is for a patented drug entitled to 5 years of marketing exclusivity under section 505(c)(3)(D)(ii) or (j)(4)(D)(ii) of the act, where the patent holder files an action for patent infringement during the 1-year period beginning 4 years after the date the patented drug was approved (and within 45 days of receiving the notice of patent certification). In this situation, FDA must extend the 30-month period by that amount of time required for 7 1/2 years to elapse from the date of approval of the patented drug. Once the 30 months, or 7 1/2 years where applicable, have expired, the applicant would have an effective approval of its drug product subject to the outcome of the pending litigation, unless the court itself orders otherwise.

If before the expiration of the 30-month or 7 1/2 -year period the court decides that any relevant patent is invalid or not infringed, approval of the ANDA or 505(b)(2) application would be made effective on the date that final judgment is entered by the court.

If before the expiration of the 30-month or 7 1/2 -year period the court decides that any relevant patent would be infringed, the approval would be made effective on the date the patent expires or on the date the court orders. If before the expiration of the 30-month or 7 1/2 -year period the court grants a preliminary injunction prohibiting an applicant from manufacture or marketing of its drug product until the court

decides the issues of patent validity and infringement and if the court later decides that the patent is invalid or not infringed, approval would be made effective on the date the court enters final judgment on the merits.

For purposes of establishing the proper effective date for an ANDA or 505(b)(2) application approval in the above situations, FDA proposes that the applicant submit to the Division of Generic Drugs (HFD-230), within 10 working days of the entry of any relevant judgment, a copy of the court order. There is a potential ambiguity in the statutory language concerning what "court" decision triggers an effective date. The agency has interpreted that language as referring to the final decision of that court from which no appeal can be or has been taken by the affected party.

FDA will issue a revised approval letter stating the effective approval date. However, an applicant may begin marketing its approved drug product on the date that final judgment is entered by the court or on any other court ordered effective date whether or not the applicant has received a revised approval letter from FDA.

2. The 180-day exclusivity period. Finally, under the proposal and the statute, if any subsequent ANDA's for the same drug product as the first drug product to be involved in a patent infringement action also contain a certification of the invalidity or noninfringement of a patent, approval of those subsequent ANDA's would not become effective until 180-days after the first commercial marketing of the drug product under the first ANDA, or until 180 days after the court has determined that the patents in dispute are invalid or not infringed, whichever is earlier. (See section 505(j)(4)(B)(iv) of the act.) This provision does not apply to 505(b)(2) applications.

FDA has concluded that the 180-day delay of subsequent ANDA's is available only to a previous applicant who has

been sued for patent infringement following its notification to the patent owner of the filing of a certification of invalidity and noninfringement. Although section 505(j)(4)(B)(iv) of the act can be interpreted in several ways, FDA believes that the structure of the provision reflects Congress' intention to provide to the first generic applicant who spends its resources to litigate the scope or validity of a patent a 180-day period free from generic competition.

The formula provided by section 505(j)(4)(B)(iv) of the act for calculating the date from which the 180-day period runs, and particularly the reference to "first commercial marketing," can be applied logically and consistently with the statutory scheme only if Congress intended the provision to apply only when the first ANDA applicant was actually sued for patent infringement. Every other exclusivity provision in the 1984 Amendments begins with date of approval of the application. Congress' decision to begin the 180-day period under section 505(j)(4)(B)(iv)(I) of the act from "the first commercial marketing of the drug," rather than from the effective date of the ANDA, serves a rational policy only if Congress contemplated a situation in which an approval of an ANDA is in effect but the applicant's decision not to market the drug deserves to be protected because a delay in marketing serves the public interest.

Such a situation occurs where, under the terms of section 505(j)(4)(B)(iii) of the act, an ANDA goes into effect 30 months after a lawsuit is filed, but the lawsuit is still pending. It serves the public interest to permit a prudent ANDA holder in that situation to stay off the market until the litigation is resolved, thereby minimizing potential damages.

As drafted, sections 505(j)(4)(B)(iv)(I) and (II) of the act carefully avoid providing an incentive for immediate marketing: the 180-day reward of exclusive marketing begins when the applicant wins the lawsuit or when the applicant actually begins marketing, "whichever is earlier." The

applicant thus does not lose any of the 180-day period by electing to stay off the market until the lawsuit is over.

If, on the other hand, section 505(j)(4)(B)(iv) of the act is interpreted to apply even if the first applicant has not been sued, dating the 180-day period from "first commercial marketing" rather than from the effective date of the ANDA approval serves no purpose. Indeed, it might provide a counterproductive incentive to the first ANDA applicant to delay marketing so as to prolong the period during which other ANDA's may not be marketed. In contrast to the delay occasioned by a prudent plaintiff in a lawsuit, this delay serves no public interest. To remove this unproductive incentive for delay, the agency would therefore consider it necessary to read into section 505(j)(4)(B)(iv)(I) of the act various additional requirements and presumptions.

Section 505(j)(4)(B)(iv) can thus be applied straightforwardly only when an applicant who seeks the 180-day period of exclusive marketing has been involved in a patent infringement lawsuit. To apply the section where there has been no lawsuit, requires either that the agency ignore the plain language of the section, essentially reading out the phrase "first commercial marketing," or that the agency assume, contrary to the goals of the 1984 Amendments, that Congress intended to create an incentive for delay in competition, without any countervailing benefit to society. Moreover, the policy embodied in the provision, of rewarding the applicant who devotes the considerable time and money necessary for patent litigation, is not served by providing 180 days of exclusive marketing to an applicant who avoids a lawsuit. Accordingly, proposed § 314.107(c) applies only when the first applicant has been sued.[2]

---

[2] Note; Subsequent to the Commissioner's signing of this document, a Federal district court reached a contrary conclusion. *See Inwood v.*

FDA has also concluded that the 180-day period of exclusivity delays approval of all generic copies of the same listed drug whose applications contain paragraph IV certifications. It has been suggested that where a formulation or composition patent is the subject of certification and lawsuit, the exclusivity granted under section 505(j)(4)(B)(iv) should delay the effective approval only of subsequent applications that raise claims of noninfringement identical or similar to those raised by the holder of the exclusivity. The legislative history of section 505(j)(4)(B)(iv) is silent as to the purpose of the provision and does not limit its applicability to subsequent applicants that receive a benefit from the first applicant's finding of noninfringement. The 180-day period can be interpreted as a reward not only for the benefit provided to subsequent ANDA applicants but for the benefit to the public of removing an obstacle to competition. Moreover, FDA lacks the expertise in patent law that would allow it to determine whether a subsequent applicant raised issues of noninfringement in common with the previous applicant. Therefore, the 180-day period is available to the applicant who resolves an issue of patent coverage, regardless of the judgment's applicability to subsequent ANDA applicants.

3. Other provisions. FDA proposes to implement other aspects of section 505(j)(4)(B)(iv) of the act as follows:

a. Date of submission. The date of submission of a prior application that contained a certification of invalidity or noninfringement will be considered the date on which the applicant submitted a substantially complete ANDA. In most cases, to be "substantially complete," an ANDA must contain data from any required bioavailability or bioequivalence studies. A required bioequivalence study is one that meets

---

Young, No. 89-0845 (D.D.C. May 12, 1989). An appeal from that decision is under consideration.

any FDA guidance document or is otherwise reasonable in design and purports to show that the drug product for which the applicant seeks exclusivity is bioequivalent to the listed drug. Neither a protocol nor a pilot study will satisfy these requirements. (An ANDA may be substantially complete without such studies only if such studies are not required to establish bioequivalence, i.e., where bioequivalence can be established through other information and the applicant has requested a waiver of the study requirements.) Although the provision could be read to permit the mere submission of the first certification of invalidity or noninfringement to delay the effective date of subsequent ANDA's, regardless of the completeness of the application, the legislative history of the 1984 Amendments makes clear that such an interpretation would be inconsistent with the purposes of the patent certification and notification scheme.

The purpose of section 505(j)(4)(B)(iv) of the act is to reward the first applicant to test the scope or validity of a patent by litigating an action for patent infringement. However, it is only the giving ofnotice to the patent owner under section 505(j)(2)(B)(ii) of the act, and not the filing of a certification of invalidity or noninfringement with FDA, that can initiate a lawsuit. The notice required by section 505(j)(2)(B)(ii) of the act must state that the applicant has submitted an ANDA "which contains data from bioavailability or bioequivalence studies." (Section 505(j)(2)(B)(ii) of the act.) The purpose of requiring a statement that the ANDA contains data from bioavailability or bioequivalence studies is to prevent applicants from testing an innovator's patent through the filing of "sham ANDA's or ANDA's that are substantially incomplete." H. Rept. 98 857, Part I, 98th Cong., 2d Sess. 24-5 (1984).

FDA believes that to fulfill the purposes of the patent provisions of the statute, the date of submission of a previous application under section 505(j)(4)(B)(iv) of the act must

therefore be the date on which the previous applicant submitted a substantially complete ANDA, and thus was in a position to notify the patent owner. As described in part V section E., supra, an ANDA that contains a certification of invalidity or noninfringement will not be accepted for review unless it contains the results of any required bioequivalence studies.

b. Delay when first application is not yet approved. If the first ANDA applicant for a listed drug is sued for patent infringement and a subsequent ANDA for the drug is submitted before the first ANDA is approved, FDA will delay the effective date of approval of the subsequent ANDA only as long as the agency remains satisfied that the first applicant is actively pursuing approval of its ANDA.

c. "First commercial marketing." "First commercial marketing" is defined as the first date of introduction or delivery for introduction into interstate commerce outside the control of the manufacturer, except for investigational use under 21 CFR Part 312, but does not include transfer of a drug product for reasons other than sale within the control of the manufacturer or application holder.

d. "Court decision." Section 314.107(c)(1)(ii) specifies as one of the two dates from which the 180 days runs "the date of a decision of the court holding the patent invalid or not infringed." This date will be the date of a final decision of a court from which no appeal can or has been taken, or the date of a settlement order or consent decree signed by a Federal judge, which enters final judgment and includes a finding that the patent is invalid or not infringed. A final adjudication on the merits is not required to trigger the 180-day period.

e. Amended certification after finding of infringement. If a final judgment is entered in an action for patent infringement finding the patent to be infringed by a drug

product that is the subject of an abbreviated new drug application, and the application contains a paragraph IV certification, the applicant should submit an amended certification, certifying under § 314.94(a)(12)(i)(A)(3) that the patent will expire on a specific date. The new certification should be submitted either as an amendment to a pending application or as a letter if the application is approved. Once the amendment or letter has been submitted, the application will no longer be considered to be one containing a paragraph IV certification.

f. Amended certification after removal of a patent from the list. If, after one or more applicants have made paragraph IV certifications on a patent, that patent is removed from the list for any reason other than because that patent has been declared invalid in a lawsuit brought by that patent owner within 45 days of receiving notice under § 314.95 any applicant with a pending application or delayed effective date who has made such a certification should submit an amended patent certification, certifying under § 314.94(a)(12)(ii) if applicable, that no relevant patents claim the drug. If other relevant patents still claim the drug, the applicant should instead submit a request to withdraw the paragraph IV certification. Once the amendment or letter has been submitted, the application will no longer be considered to be an application containing a paragraph IV certification.

* * *

APPENDIX G

Analysis to Aid Public Comment

The Federal Trade Commission has accepted for public comment an agreement and proposed consent order with Hoechst Marion Roussel, Inc. ("HMR"), Carderm Capital, L.P. ("Carderm"), and Andrx Corporation ("Andrx") to resolve the matters alleged in an administrative complaint issued by the Commission on March 16, 2000. The proposed consent order has been placed on the public record for 30 days to receive comments from interested members of the public. The proposed consent order has been entered into for settlement purposes only and does not constitute an admission by HMR, Carderm, or Andrx (collectively "the Respondents") that they violated the law or that the facts alleged in the complaint, other than the jurisdictional facts, are true. Respondents deny all other allegations of the complaint.

The Complaint

The complaint alleges that the Respondents entered into an agreement that had the tendency or capacity to restrain competition unreasonably by discouraging generic competition to Cardizem CD. Cardizem CD is a prescription drug manufactured and sold by HMR and is used to treat two chronic conditions that affect millions of Americans: hypertension (high blood pressure) and angina pectoris (chest pain). Andrx is a generic drug manufacturer that developed a generic version of Cardizem CD.

Generic drugs typically are sold at substantial discounts from the price of branded drugs. Generic drugs can have a swift marketplace impact, the complaint states, because pharmacists generally are permitted, and in some instances are required, to substitute lower-priced generic drugs for their branded counterparts, unless the prescribing physician directs otherwise. In addition, there is a ready market for generic products because certain third-party payers of prescription

drugs (e.g., state Medicaid programs and many private health plans) encourage or insist on the use of generic drugs wherever possible.

Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as "the Hatch-Waxman Act," to facilitate the entry of lower priced generic drugs while maintaining incentives to invest in new drug development. A company seeking approval from the Food and Drug Administration ("FDA") to market a new drug must file a New Drug Application ("NDA") demonstrating the safety and efficacy of its product. In order to receive FDA approval to market a generic version of a brand name drug a company must file an Abbreviated New Drug Application ("ANDA") demonstrating that its product is bioequivalent to its brand-name counterpart.

The Hatch-Waxman Act establishes certain rights and procedures in situations where a company seeks FDA approval to market a generic drug prior to the expiration of a patent or patents relating to the brand name drug upon which the generic is based. In such cases, the applicant must: (1) certify to the FDA that the patent in question is invalid or is not infringed by the generic product (known as a "paragraph IV certification"); and (2) notify the patent holder of the filing of the certification. If the holder of the patent rights files a patent infringement suit within 45 days, FDA approval to market the generic drug is automatically stayed for 30 months, under certain circumstances, unless before that time the patent expires or the patent is judicially determined to be invalid or not infringed. This automatic 30-month stay allows the patent holder time to seek judicial protection of its patent rights before a generic competitor is permitted to market its product.

In addition, the Hatch-Waxman Act provides an incentive for generic drug companies to bear the cost of patent litigation that may arise when they challenge invalid patents

or design around valid ones. Under current FDA regulations, the Act grants the first company to file an ANDA with a paragraph IV certification a 180-day period during which it has the exclusive right to market a generic version of the brand name drug. No other generic manufacturer may obtain FDA approval to market its product until the first filer's 180-day exclusivity period has expired. At the time the Respondents entered into the challenged agreement in 1997, the governing FDA regulations required that an ANDA applicant successfully defend the patent holder's patent suit in order to be entitled to this exclusivity.

Andrx was the first company to file an ANDA for a generic version of Cardizem CD. It filed a paragraph IV certification with the FDA stating its belief that the product did not infringe any valid patent covering Cardizem CD. In January 1996, HMR sued Andrx for patent infringement. The lawsuit triggered a 30-month stay of final FDA approval of Andrx's generic product, until July 1998.

According to the complaint, HMR and Andrx entered into an agreement in September 1997, in the midst of this patent lawsuit. At the time of the agreement, approximately nine months before the 30-month stay of FDA approval of Andrx's application would expire, the patent lawsuit had already been pending for twenty-one months and both sides had filed numerous dispositive motions with the trial court that had not been acted on. Also by that time, two other companies, Purepac Pharmaceutical Co. and Biovail Corporation International, had filed for FDA approval of a generic Cardizem CD product, neither of which had yet obtained tentative approval from the FDA.

HMR's forecasts, the complaint states, projected that a generic once-a-day diltiazem product would capture roughly 40 percent of Cardizem CD sales within the first year following its launch. Cardizem CD was HMR's largest selling product at the time. Accordingly, the complaint

charges, HMR sought to delay Andrx - and all other potential generic competition to Cardizem CD - from entering the market because of the threat they represented to the high profits it was making from Cardizem CD.

The complaint alleges that on September 24, 1997, HMR, Carderm, and Andrx entered into a "Stipulation and Agreement." The Stipulation and Agreement did not settle the lawsuit. Instead, under this agreement, the complaint alleges that Andrx agreed not to enter the market with its generic Cardizem CD product until the earliest of: (1) final resolution of the patent infringement litigation; (2) Andrx's exercise of an option to obtain a license from HMR in the future; or (3) notice by HMR that it would allow entry of another generic Cardizem CD product or market its own generic version of Cardizem CD. According to the complaint, Andrx also agreed to refrain from selling during the patent infringement suit any other bioequivalent or generic version of Cardizem CD. In addition, the complaint alleges that Andrx agreed not to withdraw its pending ANDA or to relinquish or otherwise compromise any right accruing under its ANDA, including its 180-day exclusivity right. In return, the complaint alleges, HMR agreed to pay Andrx $10 million per quarter during the litigation beginning when Andrx received final FDA approval of its ANDA, unless the litigation was resolved prior to that time. Under the agreement, if IBM lost the patent infringement suit it would pay Andrx an additional $60 million per year for that same time period. On September 25, 1997, the parties made public disclosures of the existence of the agreement. The Commission's complaint alleges that this agreement, at the time it was entered into, had the potential to affect Andrx's incentive to compete once it received final FDA approval.

In July 1998, upon expiration of the 30-month stay under Hatch-Waxman, Andrx received final FDA approval to market its original formulation of generic Cardizem CD that

was subject to the still on-going lawsuit with HMR. Pursuant to the terms of the Stipulation and Agreement, HMR began making quarterly payments of $10 million to Andrx.

Andrx filed a supplement to its ANDA reflecting a reformulation of its generic Cardizem CD product in September 1998. This reformulation altered the dissolution profile of the Andrx product, which was the basis of the patent dispute between Andrx and HMR. The FDA required Andrx to file a new certification and give notice to HMR of the reformulated product under the Hatch-Waxman procedures described above. Following its analysis of the reformulated product, HMR agreed that it would not assert a patent claim against the reformulated product. By June 1999, Andrx had solved the difficulties it had encountered since the summer of 1997 in consistently manufacturing commercial scale quantities of its formulations of its product in conformity with FDA regulations. Andrx received FDA approval in June 1999 to market its reformulated version of Cardizem CD. On or about the day Andrx received FDA approval of its reformulated product, the Respondents entered into a stipulation dismissing the litigation, with an agreement by Andrx not to sell its original formulation and an agreement by HMR not to sue Andrx for patent infringement on Andrx's reformulated product. The challenged agreement terminated.

On or about June 23, 1999, the federal district court dismissed the patent suit, and Andrx commenced marketing its reformulated generic Cardizem CD product, triggering its 180-day exclusivity period. At that time, Biovail Corporation International had not received tentative FDA approval for its product, and Purepac Pharmaceutical Co. had entered into a licensing arrangement with HMR for manufacture of generic Cardizem CD. Andrx's 180-day exclusivity period expired on December 19, 1999. Purepac launched its generic Cardizem CD product the next day pursuant to a license from HMR. Biovail obtained final FDA approval on December 23, 1999, and launched its product shortly thereafter.

Based on the FTC's investigation, it does not appear that there was any delay in the entry into the market of a generic version of Cardizem CD by Andrx or any other potential manufacturer, or that the conduct or agreement at issue delayed consumer access to a generic version of Cardizem CD. The agreement terminated in June 1999. It was at that time that Andrx received FDA approval to market, and commenced marketing, a reformulated generic version of Cardizem CD that HMR stipulated did not infringe any HMR patent.

The complaint alleges that the challenged agreement was not justified by countervailing efficiencies. In its complaint, the Commission alleged that the presence in the agreement of a licensing provision (permitting Andrx to obtain a license from HMR to market generic Cardizem CD in January 2000, in the event Andrx lost the patent litigation, or if another generic company obtained final FDA approval) did not justify the agreement. The complaint alleges that entry by Andrx under a license, had it occurred, likely would have been later than entry by Andrx or another generic manufacturer absent the agreement.

Finally, the complaint charges that HMR had a monopoly in the market for once-a-day diltiazem, and, that by entering into the agreement with Andrx, HMR sought to preserve its dominance by delaying the entry of Andrx and other generic companies into the market. At the time of the challenged agreement, HMR accounted for 70% of the sales of once-a-day diltiazem in the United States. Other drugs, the complaint alleges, are not effective substitutes for once-aday diltiazem because they are different in efficacy and side effects, and because of risks associated with switching patients from one treatment to another. In addition, the complaint alleges that HMR and Andrx conspired to monopolize the market for once-a-day diltiazem products. The complaint alleges that HMR and Andrx acted with specific intent that HMR

monopolize the market for once-a-day diltiazem, and entered into a conspiracy to achieve that goal. Finally, the complaint charges that the Respondents' agreement otherwise amounts to an unfair method of competition in violation of Section 5 of the FTC Act.

The Proposed Order

In a statement issued at the time of the filing of the complaint in this matter, the members of the Commission stated that cases like this one "must be examined with respect to [their] particular facts," and that the "development of a full factual record in the administrative proceeding . . . will help to shape further the appropriate parameters of permissible conduct in this area, and guide other companies and their leaf advisors."[1] Although the particular agreement challenged in the complaint has been terminated, the Commission believes prospective relief is necessary to prevent a recurrence of the types of agreements covered by the proposed order. Private agreements in which the brand name drug company (the "NDA Holder") pays the first generic to seek FDA approval (the "ANDA First Filer"), and the ANDA First Filer agrees not to enter the market, have the potential to delay generic competition and raise serious antitrust issues. Moreover, the FDA has observed that the incentives for companies to enter into such arrangements are becoming greater, as the returns to a brand name company from extending its monopoly increasingly exceed the potential economic gains to the generic applicant from its 180 days of market exclusivity.'

The proposed order strikes an appropriate balance, on a prospective basis, between the legitimate interests of the Respondents and the Commission's concerns with the

---

[1] Statement of Chairman Pitofsky, Commissioner Anthony, Commissioner Thompson, Commissioner Swindle, and Commissioner Leary concerning Abbott Laboratories and Geneva Pharmaceuticals, Inc., File No. 991-0395 (March 16, 2000).

possible competitive effects of agreements between NDA Holders and ANDA First Filers. By not imposing any broad prohibitions on the Respondents' ability to compete, the order maintains HMR's incentive to develop and sell new drug products and Andrx's incentive to develop and sell generic products that do not infringe valid intellectual property rights held by others. In addition, the order preserves Andrx's ability to decide for itself whether to market a product in the face of a claim of patent infringement, so long as such decision is otherwise lawful.

As described more fully below, the proposed order:

- bars (except in certain licensing arrangements) two particular types of agreements between brand name drug companies and potential generic competitors-restrictions on giving up Hatch-Waxman 180-day exclusivity rights and on entering the market with a non-infringing product;
- requires that interim settlements of patent litigation involving payments to the generic company in which the generic company temporarily refrains from bringing its generic product to market, be approved by the court, with notice to the Commission to allow it time to present its views to the court; and
- requires the Respondents to give the Commission written notice 30 days before entering into such agreements in other contexts.

Paragraph II prohibits two kinds of agreements between an NDA Holder and the ANDA First Filer (that is, the party possessing an unexpired right to Hatch-Waxman 180-day exclusivity). Paragraph II.A. bars agreements in which the first company to file an ANDA agrees with the NDA Holder not to relinquish its right to the 180-day exclusivity period (as interpreted by the courts at the time of the agreement). Paragraph II.B. prohibits the ANDA First Filer from agreeing

not to develop or market a generic drug product that is not the subject of a claim of patent infringement. The order recognizes, however, that even these types of agreements, in the context of certain licensing arrangements, might not raise competitive concerns. Accordingly, conduct otherwise falling within the conduct described in Paragraph II would not be prohibited where the ANDA First Filer agrees to license and introduce a competitive product to the market, its 180-day exclusivity right is not extended, and the Commission is provided notice. FDA Proposed Rule Regarding 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications, 64 Fed. Reg. 42873, 42882-83 (August 6, 1999).

Paragraph II's focus on agreements between an NDA Holder and the ANDA First Filer does not mean that the Commission believes that there is no risk of competitive harm in other types of agreements. In particular substantial competitive concerns could arise from an agreement in which a generic company (other than the ANDA First Filer) agrees with the NDA Holder to refrain from marketing a non-infringing product. Given the variety of circumstances in which the restraints may arise, however, and the possibility that some legitimate justifications might exist for such arrangements, the Commission believes that it is appropriate at this time to limit the bans in Paragraph II to the described agreements between NDA Holders and ANDA First Filers.

Paragraph III covers certain private agreements involving payments from the NDA Holder to the ANDA First Filer during patent infringement litigation. Generally, the Respondents can enter into such arrangements only if (a) the agreement is presented to the court and embodied in a court-ordered preliminary injunction, and (b) the following other conditions are met: (i) along with any stipulation for preliminary injunction, Respondents provide the court with a copy of the Commission's complaint, order, and the Analysis

to Aid Public Comment in this matter, as well as the proposed agreement; (ii) at least 30 days before submitting the stipulation to the court, they provide written notice (as set forth in Paragraph V of the order) to the Commission; and (iii) they do not oppose Commission participation in the court's consideration of the request for preliminary relief.

This part of the proposed order is designed to enhance the court's ability to assess the competitive implications of such agreements. This remedy, in addition to facilitating the court's access to information about the Commission's views, may also make the process more public and thereby may prompt other generic drug manufacturers (or other interested parties) to participate.

Paragraph IV addresses private agreements in which an ANDA First Filer agrees with the NDA Holder not to enter the market. Such situations would include agreements that are part of a final settlement of the litigation, and situations in which no litigation has been brought. In these circumstances, there may be no judicial role in ordering relief agreed to by the Respondents. Thus, the order requires that the Respondents notify the Commission at least 30 days before entering into such agreements. Such notice will assist the Commission because of the potential for competitive harm that these agreements may create. Absent the order, there may be no effective mechanism for the Commission to find out about such agreements.

The form of notice that the Respondents must provide to the Commission under Paragraphs II, III and IV of the order is set forth in Paragraph V. In addition to supplying a copy of the proposed agreement, the Respondents are required to provide certain other information to assist the Commission in assessing the potential competitive impact of the agreement. Accordingly, the order requires the Respondents to identify, among other things, all others who have filed an ANDA for a product containing the same chemical entities as the product

at issue, and the court that is hearing any relevant legal proceedings involving either party. In addition, the Respondents must provide the Commission with all documents that evaluate the proposed agreement.

The proposed order also contains certain reporting and other provisions that are designed to assist the Commission in monitoring compliance with the order and are standard provisions in Commission orders.

The order will expire in 10 years.

Opportunity for Public Comment

The proposed order has been placed on the public record for 30 days in order to receive comments from interested persons. Comments received during this period will become part of the public record. After 30 days, the Commission will again review the proposed order and the comments received and will decide whether it should withdraw from the proposed order or make the proposed order final.

By accepting the proposed order subject to final approval, the Commission anticipates that the competitive issues alleged in the complaint will be addressed. The purpose of this analysis is to facilitate public comment on the agreement. It is not intended to constitute an official interpretation of the agreement, the complaint, or the proposed consent order, or to modify their terms in any way.

APPENDIX H

STIPULATION AND AGREEMENT

Stipulation and Agreement, dated September 24, 1997, between Hoechst Marion Roussel, Inc. and Cardern Capital L.P. (collectively, HMRI) and Andrx Pharmaceuticals, Inc. (Andrx);

WHEREAS, HMRI is the holder of United States patent No. 5,470,584 ('584 Patent), which patent HMRI asserts covers the controlled release diltiazem hydrochloride formulation which is marketed in the United States under the trademark Cardizem® CD; and

WHEREAS, Andrx has developed a controlled release diltiazem hydrochloride formulation which it asserts is bioequivalent to Cardizem® CD and, pursuant to 21 U.S.C. § 355(j) has submitted and amended an abbreviated new drug application (ANDA) to the United States Food and Drug Administration (FDA) in order to obtain the right to sell that product (the Andrx Product) in the United States; and

WHEREAS, HMRI has filed a Complaint against Andrx in the United States District Court claiming that the Andrx Product infringes the '584 patent, which case is pending in the Southern District of Florida as Case Number 96-06121 (the Patent Infringement Action); and

WHEREAS, both parties recognize that until the issues of whether the Andrx Product infringes the '584 patent and whether the '584 patent is valid and enforceable are resolved in a final and unappealable order or judgment (Final Judgment) each party could take actions during the pendency of the Patent Infringement Action which could have significant financial repercussions; and

WHEREAS, HMRI believes that the market for diltiazem hydrochloride and the consumers of diltiazem hydrochloride

could be harmed in the event that an infringing or nonbioequivalent product were brought to market; and

WHEREAS, HMRI has asserted that it intends to seek an injunction barring the marketing, distribution or sale of the Andrx Product prior to the entry of Final Judgment on HMRI's claims in the Patent Infringement Action; and

WHEREAS, HMRI has also asserted that it intends to seek substantial damages and trebled damages for any marketing of the Andrx Product before the entry of Final Judgment; and

WHEREAS, Andrx recognizes that it could lose a substantial investment were it to move forward to market the Andrx Product following the date on which the FDA's approval of the Andrx Product under 21 U.S.C. §355(j) becomes effective (FDA Approval) but before the entry of Final Judgment and were HMRI successful in obtaining an injunction blocking the distribution and sale of the product; and

WHEREAS, Andrx also recognizes that the damages could be potentially ruinous were Andrx to bring the Andrx Product to market and were HMRI to prevail in the Patent Infringement Action; and

WHEREAS, Andrx also believes that if it were to refrain from selling the Andrx Product until after Final Judgment is rendered in the Patent Infringement Action and it prevails in the Patent Infringement Action, then it will have lost substantial revenues from the Andrx Product; and

WHEREAS, Andrx is desirous of bringing a bioequivalent or generic form of Cardizem® CD to the market; and

WHEREAS, the parries intend to fully and vigorously litigate the infringement and validity issues underlying the Patent Infringement Action, but wish to reduce the risks and losses which could result from an adverse decision with respect to damages.

NOW THEREFORE, in consideration of the foregoing and for other good and valuable consideration, and the mutual covenants set forth herein, the parties agree as follows:

1. Effect of Recitals:

   The recitals set forth above are true and correct and are incorporated herein by reference.

2. Obligation to Maintain Status Quo:

   (A). Pending the entry of Final Judgment, the parties agree to maintain the status quo with respect to the commercial sale of the Andrx Product in the United States. Andrx agrees not to commence the commercial sale of the Andrx Product or other bioequivalent or generic version of Cardizem® CD in the United States directly or indirectly until the entry of Final Judgment, or until it obtains a license from HMRI pursuant to paragraphs 5, 6, and 7 of this Stipulation and Agreement, or until Andrx receives the notice required by Paragraph 5 of this Stipulation and Agreement, whichever is the first to occur. Andrx further agrees that during the pendency of the Patent Infringement Action, it will diligently prosecute the ANDA for the Andrx Product and will not relinquish or otherwise compromise any right accruing thereunder or pertaining.thereto.

   (B). HMRI agrees not to seek further preliminary injunctive relief against Andrx in this litigation or otherwise until the entry of Final Judgment. HMRI further agrees that for the period beginning on April 1, 1998 and ending upon the termination of this Stipulation and Agreement or the termination of any licensing agreement entered hereunder, whichever is later, HMRI will provide Andrx with a copy of any changes it proposes to the FDA with respect to the package insert and the immediate container label for Cardizem® CD within 10 days of the date upon which such proposed changes are transmined to the FDA. HMRI further

agrees that it will notify Andrx of any proposed changes which may be pending before the FDA as of April l, 1998.

HMRI further agrees to notify Andrx in writing of any labeling change which is approved by the FDA with respect to Cardizem® CD within 10 days of receiving notification of such approval.

(C). Andrx agrees that it will dismiss, without prejudice, its antitrust and unfair competition counterclaims in the Patent Infringement Action (including but not limited to counts III through VI and counts XI through XV of said counterclaim) within 30 days of the execution of this Stipulation and Agreement. Andrx further agrees that as between the parties to this Stipulation and Agreement, such dismissal shall be with prejudice as of the date that Final Judgment becomes effective, provided that HMRI has fully complied with the terms of this Stipulation and Agreement.

(D). Both parties agree that neither will apply to the court in the Patent Infringement Action for an order increasing or decreasing the thirty (30) month period provided for by 21 U.S.C. §3550)(4)(B)(iii).

3. Los Profit Payments:

(A). For the purposes of this Stipulation and Agreement, the parties stipulate that the profits that Andrx would have realized from the sale of the Andrx Product would be $100 million per year after FDA Approval.

(B). If Final Judgment determines that the '584 patent is invalid or unenforceable or that the Andrx Product does not infringe said patent, HMRI shall pay Andrx an amount, calculated at the stipulated rate of $100 million per year and prorated for fractions of a year, for the period beginning upon FDA Approval and ending on the date that Final Judgment becomes effective. (For the purposes of this Stipulation and Agreement, the Effective Date of Final Judgment shall mean

the later of the date of final disposition in respect of said Final Judgment (or order, as the case may be) or the expiration of the period to appeal or seek review of said disposition, order or Final Judgment.) Said amount shall be reduced solely by an amount equal to the amounts actually paid to Andrx by HMRI pursuant to Paragraph 4(A) below.

(C). In the event that HMRI provides Andrx with notice pursuant to Paragraph 5(B) of this Stipulation and Agreement, the end of the period described in Paragraph 3(B) above shall be the earlier of: (1) the date Andrx effects its first commercial sale of the Andrx Product; or (2) the date HMRI or its licensee effects its first commercial sale of a generic or bioequivalent form of Cardizem® CD, provided that the first such sale by HMRI or its licensee occurs after the expiration of the notice period described in Paragraph 5(B).

(D). In the event that Andrx exercises its option to acquire a license pursuant to Paragraph 6 (A)(ii) of this Stipulation and Agreement, the end of the period described in Paragraph 3(B) above shall be the date upon which said license agreement becomes effective.

(E). Andrx shall prepare and forward an invoice for the amount due from HMRI pursuant to this Paragraph and that invoice shall be payable and paid to Andrx within 30 days of the date of the invoice.

4. Interim Payments:

(A). For the period beginning upon FDA Approval and ending on the Effective Date of Final Judgment, Andrx shall be entitled to receive nonrefundable interim payments from HMRI of $40 million per year, payable quarterly. Within 10 days after FDA Approval, HMRI shall pay to Andrx a prorated amount for the period between that effective date and the end of that calendar quarter. On the first day of each calendar quarter after that effective date, HMRI shall pay to

Andrx the full $10 million quarterly payment due to Andrx under this Paragraph.

(B). In the event that HMRI provides Andrx with notice pursuant to Paragraph 5(B) of this Stipulation and Agreement, the end of the period described in Paragraph 4(A) shall be the date upon which the applicable written notice period described in Paragraph 5(B) expires or the date Andrx effects its first commercial sale of the Andrx Product, whichever is earlier.

(C). In the event that Andrx exercises its option to acquire a license pursuant to Paragraph 6 (A)(ii) of this Stipulation and Agreement, the end of the period described in Paragraph 4(A) above shall be the date upon which said license agreement becomes effective.

5. License:

HMRI hereby grants, and warrants it has the right to grant, to Andrx an irrevocable option to acquire a license (or sublicense as the case may be) to all intellectual property which HMRI owns or controls that Andrx may need to sell, market and distribute the Andrx Product in the United States, its territories and possessions, including the Commonwealth of Puerto Rico. (HMRI agrees that it shall not sell, assign or otherwise voluntarily divest itself of said intellectual property during the term of this Stipulation and Agreement in a way which would interfere with or otherwise frustrate Andrx's right to acquire a license under either Paragraphs 5 or 6 of this Stipulation and Agreement.) Such license shall be non-exclusive.

(A). In the event that Andrx previously has taken a license under Paragraphs 6(A)(i) or 6(A)(ii) of this Stipulation and Agreement. HMRI shall have no obligation to notify Andrx of HMRI's intention to either license said intellectual property to any other party (either directly or indirectly, including, but not limited to. an agreement not to

enforce said intellectual property against the other party) for the purposes of selling a bioequivalent or generic version of Cardizem® CD or utilize said intellectual property (directly or through a subsidiary) for the purpose of selling its own bioequivalent or generic version of Cardizem® CD in its own right.

(B). In the event that Andrx has not taken a license under Paragraphs 6(A)(i) or 6(A)(ii) of this Stipulation and Agreement and HMRI elects to either license said intellectual property to any other party (either directly or indirectly, including, but not limited to, an agreement not to enforce said intellectual property against the other party) for the purposes of selling a bioequivalent or generic version of Cardizem® CD or utilize said intellectual property (directly or indirectly through a subsidiary or any other entity) for the purpose of selling its own bioequivalent or generic version of Cardizem® CD in its own right, then HMRI shall give Andrx written notice prior to the date upon which the third party licensee is authorized to make its first commercial sale or the date of HMRI's first commercial sale as required in the following schedule:

(i). If the date upon which the third party licensee is authorized to make its first commercial sale or HMRI's first planned sale arises on or before July 1, 1998 - 360 days prior written notice is required.

(ii). If the date upon which the third party licensee is authorized to make its first commercial sale or HMRI's first planned sale arises after July 1, 1998 and on or before December 31, 1998 -180 days prior written notice is required.

(iii). If the date upon which the third party licensee is authorized to make its first commercial sale or HMRI's first planned sale arises on or after January 1, 1999 and

on or before March 31, 1999 -120 days prior written notice is required.

(iv). If the date upon which the third party licensee is authorized to make its first commercial sale or HMRI's first planned sale arises on or after April 1, 1999 and on or before June 30, 1999 - 90 days prior written notice is required.

(v). If the date upon which the third party licensee is authorized to make its first commercial sale or HMRI's first planned sale arises after June 30, 1999 - 30 days prior written notice is required.

(C). The notice provided in Paragraph 5(B) above shall identify, by name, the third party licensee or the HMRI entity authorized to sell a bioequivalent or generic version of Cardizem® CD and shall specify the date upon which the third party licensee is authorized to make its first commercial sale or the date HMRI's first commercial sale is contemplated.

(D). Except as expressly provided in this Stipulation and Agreement, HMRI expressly retains all rights under said intellectual property.

6. Time to Exercise Option to Obtain License:

(A) The option referred to in Paragraph 5 above must be exercised. if at all, at one of the three opportunities set forth below.

(i) By no later than the period beginning on the Effective Date of Final Judgment and ending 30 days thereafter.

(ii) In the event that Final Judgment is not entered before the earlier of:

(a) a date 18 months following FDA Approval; or,

(b) the date upon which FDA approval for a third party to make and market a bioequivalent or generic version of Cardizem® CD becomes effective.

Andrx may exercise said option at any time beginning on the earlier of these dates and ending on the date 30 days after the Effective Date of Final Judgment.

(iii) In the event that HMRI notifies Andrx of its intent to license said intellectual property to any other party for the purposes of selling a bioequivalent or generic version of Cardizem® CD, or of its intent to use said intellectual property (directly or indirectly through a subsidiary or any other entity) for the purpose of selling its own bioequivalent or generic version of Cardizem® CD, Andrx may exercise said option at any time beginning on the date it receives said notification and ending on the Effective Date of Final Judgment.

(B). Except as regards the license fees and royalty rates set forth below, the terms of the license shall be negotiated in good faith by the parties and shall allow Andrx to sell the Andrx Product as a bioequivalent or generic version of Cardizem® CD. Andrx shall be authorized to sell the Andrx Product during such negotiations and prior to the execution of a formal license agreement.

7. License Fee and Royalties:

As set forth below, Andrx agrees to pay HMRI a license fee at the time it acquires a license pursuant to this Stipulation and Agreement as well as royalties based upon the "net receipts" based upon the sales of the licensed products. For the purpose of this Stipulation and Agreement and of any license entered into by the parties pursuant to this Stipulation and Agreement, the term "net receipts" shall mean gross receipts less deductions relating to returns, shelf stock allowances, discounts, rebates and similar adjustments.

(A). In the event that Andrx acquires the license pursuant to Paragraph 6(A)(i) of this Stipulation and Agreement, the license fee is S60 million and the royalty is 20% on net receipts.

(B). In the event that Andrx acquires the license pursuant to Paragraph 6(A)(ii) or Paragraph 6(A)(iii) of this Stipulation and Agreement. the initial license fee is $30 trillion and the royalty is 10% on net receipts collected prior to the Effective Date of Final Judgment.

(i). If Final Judgment determines that the '584 patent is invalid or unenforceable or that the Andrx Product does not infringe said patent, HMRI shall refund said license fee by paying to Andrx S30 million and shall refund all royalty payments made to HMRI by Andrx under the license within 30 days of the Effective Date of said Final Judgment. and the license shall be terminated on the Effective Date of Final Judgment.

(ii). Unless Final Judgment determines that the '584 patent is invalid or unenforceable or that the Andrx Product does not infringe said patent, Andrx shall pay HMRI an additional license fee of S30 million within 30 days of the Effective Date of Final Judgment and thereafter pay HMRI a royalty of 20% on net receipts.

8. Final Judgment and Termination:

(A). In the event that HMRI dismisses the Patent Infringement Action prior to the Effective Date of Final Judgment, such dismissal shall be deemed to be as between the parties to this Stipulation and Agreement, a Final Judgment that the '584 patent is invalid or unenforceable or that the Andrx Product does not infringe said patent and said Final Judgment will be deemed to be effective on the date 90 days following the date upon which such dismissal becomes effective. HMRI agrees that such dismissal shall be with prejudice and shall eliminate HMRI's right to refile such an

action pursuant to Paragraph 8(C). If Andrx has taken a license under either Paragraph 6(A)(ii) or 6(A)(iii) of this Stipulation and Agreement, Andrx's obligation to pay royalties under the license shall terminate as of the date such dismissal is entered (not the deemed Effective Date of Final Judgment), and Paragraph 7(B)(i) shall apply and Paragraph 7(B)(ii) shall not apply.

(B). It is understood by the parties that in addition to the specific obligations set forth in Paragraph 2 of this Stipulation and Agreement, Andrx agrees that it may not transfer, sell or assign any right to obtain a license pursuant to Paragraphs 5 and 6 of this Stipulation and Agreement or any rights granted to Andrx pursuant to a license issued under said paragraphs to any other party without the express written consent of HMRI (a change in the ownership or control of Andrx's stock shall not require HMRI's consent), and, subject to subparagraph (iv) below, Andy. may not, prior to the Effective Date of Final Judgment, withdraw the ANDA that it has submitted to the FDA for the Andrx Product.

(i). In the event that Andrx violates its obligations under Paragraph, 2; transfers, sells or assigns any rights granted to Andrx by HMRI pursuant to Paragraphs 5 and 6 of this Stipulation and Agreement or pursuant to any license issued under said paragraphs to any other party without the express written consent of HMRI (a change in the ownership or control of Andrx's stock shall not require HMRI's consent), or, prior to the Effective Date of Final Judgment, withdraws the ANDA that it has submitted for the Andrx Product, then Andrx shall pay HMRI an amount equal to the amount of all payments that have been paid to Andrx pursuant to this Stipulation and-Agreement, and this Stipulation and Agreement shall be terminated.

(ii). Before HMRI may seek termination of this Stipulation and Agreement and the return of monies paid

to Andrx pursuant to this Subparagraph 8(B)(i), HMRI shall provide express written notice to Andrx specifying the obligation which, in HMRI's opinion, Andrx has not fulfilled, the specific manner in which each such obligation has not been fulfilled, and the specific conduct by Andrx that, in HMRI's opinion, will cure the asserted default. In the event that Andrx cures the alleged non-fulfillment identified by HMRI within 30 days of receiving such notice (or such other longer period as HMRI in writing expressly consents), such cure will be deemed full compliance (retroactive to the date of the first asserted default) an(. this Stipulation and Agreement will remain in full force and effect.

(iii). If Andrx has taken a license under either Paragraphs 6(A)(ii) or 6(A)(iii) of this Stipulation and Agreement, termination of this Stipulation and Agreement as contemplated under Paragraph 8(B)(i) shall not terminate any license previously granted to Andrx pursuant to Paragraph 5 and, with respect to license fees and royalty payments, Paragraph 7(B)(ii) shall apply and Paragraph 7(B)(i) shall not apply.

(iv). Nothing in this Stipulation and Agreement shall be construed as prohibiting or limiting Andrx's right to amend or modify the ANDA that it has filed with respect to the Andrx Product so long as such amendment or modification shall not require the withdrawal of the existing ANDA and/or submission of a new ANDA and shall otherwise be consistent with Andrx's obligation to diligently prosecute its ANDA before the FDA as set forth in Paragraph 2 of this Stipulation and Agreement. For all purposes of this Stipulation and Agreement, the term "Andrx Product" shall mean the product Andrx intends to sell pursuant to the ANDA on file with the FDA and as said ANDA may be amended consistent with this subparagraph.

(C). Notwithstanding any other provision of this Stipulation and Agreement, in the event that there is a final unappealable determination in the Patent Infringement Action that does not determine either (1) that the '584 Patent is valid and enforceable and the Andrx Product infringes said patent; or (2) that the '584 patent is invalid or unenforceable and/or that the Andrx Product does not infringe said patent, such determination shall be deemed to constitute, for all purposes in this Stipulation and Agreement, a Final Judgment that the '584 patent is invalid or. unenforceable or that the Andrx Product does not infringe said patent unless HMRI notifies Andrx in writing within 30 days of the date of such determination that it continues to believe that the Andrx Product infringes the '584 Patent and that it will seek to enforce the '584 patent by refiling its action at an appropriate time in an appropriate forum and refiles its action no later that 30 days following the later of either: (1) FDA Approval; or, (2) the date upon which the final unappealable determination referenced above in this Paragraph is entered. Andrx agrees that it will not seek to block or otherwise frustrate HMRI's efforts to refile its action in this manner in a timely fashion provided that nothing herein shall be deemed to constitute a waiver by Andrx of any defenses, including the defense of preclusion, that it may have available in such refilled action. In the event HMRI provides the notice set forth above and refiles its action within the time frames herein established, such renewed action shall constitute the Patent Infringement Action for the purposes of the Stipulation and Agreement and the parties' respective obligations and rights under this Stipulation and Agreement shall continue uninterrupted and unimpaired as though no final, unappealable determination had been entered. In the event HMRI does not provide the notice set forth above or does not ref refile its action within the time frames herein established, Final Judgment shall be deemed to have been entered on the expiration of the period for HMRI to issue such notice, if it has not done so, or the

expiration of the period in which it was required to refile such action if notice was provided, and for the purposes of this Stipulation and Agreement, such date shall be deemed as the Effective Date of Final Judgment. In the event that Final Judgment is deemed entered pursuant to this paragraph, it shall, as between the parties to this Stipulation and Agreement, constitute a final conclusive and unappealable determination that the '584 patent is invalid or unenforceable or that the Andrx Product does not infringe said patent.

(D). Notwithstanding any other provision of this Stipulation and Agreement, in the event that prior to a Court determining the issues of the validity of the '584 patent and whether the Andrx Product infringes that patent, Andrx in writing stipulates or, in open court and on the record, concedes that the '584 patent is valid and that the Andrx Product infringes said patent, Andrx shall repay to HMRI an amount equal to the amount of all payments that have been paid to Andrx pursuant to this Stipulation and Agreement, and this Stipulation and Agreement shall be terminated.

9. Use of Agreement:

Except as otherwise required by law or as otherwise may be requested by the court in the Patent Infringement Action, the terms and existence of this Stipulation and Agreement shall be kept confidential. This Stipulation and Agreement and any drafts thereof or any documents or records pertaining thereto or information derived therefrom shall not be introduced into evidence in the Patent Infringement Action or any other litigation for any purpose.

10. Effect of Agreement:

The parties represent and warrant that this Stipulation and Agreement constitutes their valid and legally binding obligations and shall be binding upon and inure to the benefit of the parties hereto and their successors and assigns. Except as otherwise provided in Paragraph 8(B), this Stipulation and

Agreement may not be assigned without the express written consent of the other party. However, nothing in this Paragraph or this Stipulation and Agreement shall restrict Andrx's right to assign its right to receive income under this Stipulation and Agreement.

11. Applicable Law—Consent to Jurisdiction:

The parties hereto expressly agree that all the terms and provisions hereof shall be construed under the laws of the State of Florida as now adopted or as may be hereafter amended, without giving effect to any conflict of law or choice of law provision or rule. In the event of a dispute between the parties as to the interpretation, application or effect of this Stipulation and Agreement, the parties agree that any litigation arising out of such dispute shall be filed and venue shall be conclusively laid in the United States District Court for the Southern District of Florida, and both parties expressly consent to personal jurisdiction in that forum for the purposes of resolving said dispute.

12. Entire Agreement:

This Stipulation and Agreement constitutes the entire agreement of the parties hereto with respect to the matters set forth herein and supersedes any prior understanding or agreement, oral or written, with respect thereto.

13. Nonpayment:

Any amounts not paid when due shall thereafter bear interest at 18% per annum and all costs and expenses, including reasonable attorneys' fees, incurred in connection with the enforcement of this Stipulation and Agreement shall be paid to the prevailing party by the nonprevailing party, upon demand.

IN WITNESS WHEREOF, the parties hereto have caused this Stipulation and Agreement to be executed by their duly authorized representatives on the date first written above.

Hoechst Marion Roussel, Inc.

By /s/ Peter W. Ladell

Name PETER W. LADDELL

Title Chief Operating Officer

Andrx Pharmaceuticals, Inc.

By Chih-Ming J. Chen, Ph.D.

Name CHIH-MING J. CHEN, Ph.D.

Title President

Cardem Capital L.P.

By /s/ Dirk Kruse

Name DIRK KRUSE

Title Authorized Representative